THE RELATIONSHIP OF PSYCHOLOGICAL AND PERSONALITY FACTORS TO POST-CONCUSSIVE SYMPTOMS (PCS) IN MILD TRAUMATIC BRAIN INJURY (MTBI) PATIENTS

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LIST OF ABBREVIATIONS

ACRM	American Congress of Rehabilitation Medicine
AD	Alzheimer's disease
ATP	Adenosine triphosphate
BDI-II	Beck Depression Inventory 2nd edition
CT	Computed tomography
CVMT	Continuous visual memory test
DAI	Diffuse axonal injury
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders 4th edition
GCS	Glasgow Coma Scale
ICD-10	International Classification of Diseases 10th edition
IES	Impact of events scale
MCI	Mild cognitive impairment
MMPI	Minnesota Multiphasic Personality Inventory
MS	Multiple sclerosis
MTBI	Mild traumatic brain injury
NEO-FFI	Neuroticism-Extroversion-Openness Five Factor Inventory
NNI	National Neuroscience Institute
NUS	National University of Singapore
LOC	Loss of consciousness
PHIQ	Philadelphia head injury questionnaire
PCS	Post-concussive symptoms
PTA	Post-traumatic amnesia
PTSD	Post-traumatic stress disorder
RAVLT	Rey auditory verbal learning test
RPQ	Rivermead post-concussive symptoms questionnaire
SDMT	Symbol digit modalities test
STAI	State-Trait Anxiety Inventory
TBI	Traumatic brain injury
TOMM	Test of memory malingering
WMS-III	Weschler Memory Scale 3rd edition

Thesis Overview

Post-concussive symptoms (PCS) represent a constellation of somatic, cognitive and psychological complaints including headache, dizziness, fatigue, impaired memory problems, attentional dysfunction and personality changes that occur following a mild traumatic brain injury (MTBI). Such symptoms usually present within one to two weeks post-injury and resolve within three months, however, for some they persist beyond six months. Research has shown that the emergence, severity and duration of post-concussive symptoms (PCS) and persistent PCS (PPCS) are influenced by both injury (mostly neurological) and non-injury (mostly psychological) factors. However, the relative contributions of these factors, particularly the role of non-injury factors has not been comprehensively investigated.

This thesis sought to elucidate the role of injury and non-injury factors in PCS and PPCS using a series of established measures in neurocognitive, personality and psychological (trait and state) domains. The findings showed that mild traumatic brain injury was associated with significantly greater dispositions toward trait anxiety, neuroticism and locus of control, as well as state depression and anxiety. Patients with moderate-severe PCS demonstrated higher scores on all personality and psychological measures except locus of control relative to mild PCS or no PCS patients at two months post-injury (baseline assessment) and five months post-injury (follow-up assessment). There was a positive linear relationship between both personality and psychological variables and PCS severity. In addition, trait anxiety, neuroticism and depression were greater in persistent PCS (PPCS) compared to recovered PCS patients at five months post-injury. In contrast, the majority of injury factors did not predict PCS and persistent PCS.

In sum, non-injury factors such as personality and psychological variables appear to make a significant contribution to the manifestation and maintenance of PCS compared to injury factors. The clinical implications of the findings are discussed. The present study highlights the importance

of anxiety and associated personality and psychological disorders in the expression and persistence of PCS.

CHAPTER 1: OVERVIEW OF MILD TRAUMATIC BRAIN INJURY

Traumatic brain injury (TBI) is one of the leading public health concerns of the industrialized world (Coronado, Johnson, Faul & Kegler, 2006). An approximated 10 million TBI cases worldwide result in hospitalization or deaths annually (Langlois, Rutland-Brown & Wald, 2006). Global health estimates predict the prevalence of traumatic brain injury cases to be more than 57 million, however, the number of people living with head injury-related disabilities is relatively unknown (Murray & Lopez, 1996). Increasingly, TBI is the prevailing cause of disability and death among young people (Coronado et al., 2006).

In the United States alone 1.4 million to 3 million cases of traumatic brain injury occur; and around 1 million people are treated in hospital emergency departments, 290,000 are hospitalized and 51,000 do not survive (Rutland-Brown, Langlois, Thomas & Xi, 2006). In Singapore, TBI accounts for half of all trauma-related deaths and has emerged as the fifth highest killer in the country among adults aged forty and below (Lee, Seow & Ng, 2006).

1.1 Defining And Diagnosing Mild Traumatic Brain Injury (MTBI)

Mild traumatic brain injury (MTBI) is the least severe in the spectrum of traumatic brain injury (Stein, 1996). Recent literature suggests that MTBI is considerably different from moderate and severe head injuries and should have a classification system and care regime of its own for effective injury management and treatment (McCrea, 2008). As a result, many classification systems, definitions and diagnostic criteria have emerged (Kibby & Long, 1996).

The majority of classification systems use the Glasgow Coma Scale (GCS) score, length of loss of consciousness (LOC) and length of post-traumatic amnesia (PTA) as indicators of the severity of MTBI. The GCS consists of three domains for measuring neurological status;

namely, motor functioning, verbal responding and voluntary eye opening (or eye opening due to external stimuli) (Jennett & Teasdale, 1981; Stein, 1996). The lowest achievable score is 3 and the highest is 15. A score of 3 to 8 indicates severe head injury, 9 to 12 a moderate head injury and 13 to 15 a mild head injury. The GCS together with PTA and LOC are important in categorizing an MTBI in the acute post-injury phase, however, beyond that their utility is limited.

One of the most cited definitions and criteria for MTBI is that of the American Congress of Rehabilitation Medicine (ACRM) and its definition of MTBI is a person who has had a traumatically induced physiological disruption of brain function, as manifested by at least one of the following (Kay et al., 1993):

1. Any period of loss of consciousness
2. Any loss of memory for events immediately before or after the accident
3. Any alteration in mental state at the time of the accident (e.g., feeling dazed, disoriented, confused); and,
4. Focal neurological deficit(s) that may or may not be transient

But where the severity of the injury does not exceed the following:

1. Loss of consciousness (LOC) of 30 minutes
2. After 30 minutes, an initial Glasgow Coma Scale (GCS) score of 13-15; and
3. Posttraumatic amnesia (PTA) not greater than 24 hours

The ACRM definition and criteria for mild traumatic brain injury offer a classification that captures the core clinical features of MTBI and has been widely accepted in the mild traumatic brain injury literature as neither too restrictive nor inclusive. More recently, Carroll et al. from the World Health Organization (WHO) Task Collaborative Centre Task Force on Mild

Traumatic Brain Injury reviewed the definitions of MTBI utilized in research studies and concluded that there were substantial discrepancies (2004). In an attempt to create more standardized criteria, WHO advanced the ACRM definition. The operational definition of WHO is as follows (as cited in Ruff et al., 2009):

MTBI is an acute brain injury resulting from mechanical energy to the head from external physical forces. Operational criteria for clinical identification include: (i) 1 or more of the following: confusion or disorientation, loss of consciousness for 30 minutes or less, post-traumatic amnesia for less than 24 hours, and/or other transient neurological abnormalities such as focal signs, seizure, and intracranial lesion not requiring surgery; (ii) Glasgow Coma Scale score of 13–15 after 30 minutes post-injury or later upon presentation for healthcare. These manifestations of MTBI must not be due to drugs, alcohol, medications, caused by other injuries or treatment for other injuries (e.g. systemic injuries, facial injuries or intubation), caused by other problems (e.g. psychological trauma, language barrier or coexisting medical conditions) or caused by penetrating craniocerebral injury.

Both ACRM and WHO definitions identify the same four diagnostic criteria, that is, GCS score, length of PTA, duration of LOC and finally neurological abnormalities. Only two differences emerge. The first is that WHO simplified the ACRM definition by changing the wordings “dazed, disoriented or confused” to just “confusion and disorientation”. The second difference is that WHO limited the focal neurological deficits to just transient ones not requiring surgery. The option of non-transient focal neurological deficits is omitted. These two changes allow for a more focused operational definition.

1.2 Epidemiology and Causes of Mild Traumatic Brain Injury (MTBI)

It is estimated that mild traumatic brain injury accounts for 70 to 90% of all documented TBIs (Cassidy et al., 2004; Rose, 2005). Furthermore, 100 to 300/100,000 of the population suffer from MTBI treated in hospitals (Carroll et al., 2004). However, this figure is likely to be an underestimate due to diverse definitions, methodological shortcomings and variable techniques in investigating MTBI (McCrea, 2008). In addition, MTBI often manifests as an uncomplicated concussion, therefore, the majority of people sustaining a mild head injury fail to actively seek medical help. Consequently, the true incidence of MTBI in the population is hypothesized to be 500/100,000 in the population (McCrea, 2008). People who are susceptible to mild traumatic brain injury are typically very young (5 years and younger) or very old (74 years and older) and are predominantly males (Bazarian et al., 2005). The primary causes of MTBI are motor vehicle accidents (45%), falls (30%), occupational accidents (10%), recreational accidents (10%) and assaults (5%) (Weight, 1998).

In Singapore, reports on the number of MTBI cases are unavailable. However, the Mild Head Injury Clinic at the National Neuroscience Institute, Tan Tock Seng Hospital, Singapore treated approximately 24 MTBI patients weekly for follow-up appointments from October 2009 to December 2009 as stated by B. T. Ang (personal communication, January 5, 2010). 8451 motor vehicle accidents and 10964 casualties were documented in 2008 compared to 8325 accidents and 10566 casualties in 2007 (Singapore Police Force, 2008). Therefore, extrapolating from the substantial number of motor vehicle accidents and the fact that a relatively low speed motor vehicle accident can result in MTBI, the number of MTBI cases in Singapore appears to be comparable to other countries.

1.3 Course and Outcome Of MTBI

A wide range of cognitive, psychological/behavioural and physical symptoms known as post-concussive symptoms (PCS) are typically experienced after mild traumatic brain injury. Such symptoms are mostly transient in both adult and children populations with recovery within one to two weeks post-injury, but for some they span several more weeks (Carroll et al., 2004). Cognitive impairments usually manifest as difficulties in memory, attention and concentration. Language and visual perception deficits are usually transient or rarely recognized. Executive functioning skills such as complex and abstract reasoning, planning, insight and judgment, problem solving, organization and information processing are vulnerable after mild traumatic brain injury (Ashman, Gordon, Cantor, & Hibbard, 2006). The psychological/behavioural symptoms after mild traumatic brain injury are associated with personality changes including impulsivity, aggression, anxiety, depression, altered emotional control and sexual functioning, mood disorders and social disinhibition (Crisp, 1992; NIH, 1998). However, whilst many neuropsychological studies have focused on cognitive and emotional aspects of mild traumatic brain injury, an extensive review based on 120 studies by the World Health Organization (WHO) Collaborating Centre Task Force on MTBI showed that headache, blurred vision and dizziness are the most cited symptoms after MTBI (Cassidy et al., 2004). Most of the symptoms following MTBI resolve within 3 months (McCrea, 2008), however, some people can have ongoing issues. For example while patients afflicted with milder MTBI (for example GCS of 15, no LOC) have higher return-to-work rates than those with more severe degrees of MTBI (for example GCS 13-14, positive LOC) (Iverson, Lange, Gaetz & Zasler, 2006) at least one other well-controlled study suggests that up to 41% of people unemployed at the time of their MTBI are highly unlikely to return to work within six months of their injury (Dikmen et al., 1994). The long term consequences of MTBI can also lead to complications such as movement

disorder, seizures, headaches, occasional visual deficits and sleep disorders (Ashman et al., 2006; NIH, 1998). There is also evidence indicating that repeated concussions may lead to mild cognitive impairment (MCI) and Alzheimer's Disease (AD) (Guskiewicz et al., 2005). Guskiewicz and colleagues have also found a relationship between an increased risk of developing clinical depression in one's lifetime and a history of repetitive concussions (2007).

Post-concussive symptoms (PCS) experienced after MTBI can sometimes persist beyond the stipulated recovery period for a small subset of MTBI afflicted individuals. The reasons for such persistence of symptoms remain unclear. However, it has been established that prolonged experience of these debilitating symptoms impact the quality of social interaction and functioning of individuals which affects interpersonal relationships among family, friends and the workplace (Crisp, 1992). In some cases, there is increased risk for suicide, divorce, unemployment, substance abuse and economic strain (NIH, 1998).

1.4 Chapter Summary

It is clear that mild traumatic brain injury is a serious health problem that is relatively common, has heterogeneous causes, and shows a particular affinity towards the young and old in the age spectrum. Studies pertaining to the course and outcome of MTBI demonstrate a negative relationship between the duration of symptoms experienced post-injury and functional outcome with persisting symptoms resulting in worse functional outcome in terms of individual competence, quality of relationships and work performance. The long-term consequences of MTBI result in physical, neurological and psychological problems if not managed properly. The implications of persisting post-concussive symptoms have serious consequences in the quality of life of MTBI afflicted individuals

CHAPTER 2: POST-CONCUSSIVE SYMPTOMS

Post-concussive symptoms (PCS) represent a constellation of somatic, cognitive and psychological complaints experienced following an MTBI and have been the subject of controversy and intense debate in neurology, psychiatry and neuropsychology for decades. Post-concussive symptoms include headache, dizziness, fatigue, irritability, forgetfulness, impaired memory and concentration, insomnia, lowered tolerance for noise and light, photophobia, visual distortions, depression and personality changes (Legome, Alt & Wu, 2009). The debate and controversy revolves around whether persistent symptoms of PCS are due to neurological, psychological or other non-injury related factors (McCrea, 2008). While a lack of evidence has hampered a satisfactory empirical conclusion to date, research pertaining to the natural history of MTBI has provided some elucidation (Iverson, Zasler & Lange, 2006).

Post-concussive symptoms usually present within one to two weeks post-injury and resolve within three months, however, for some they persist beyond six months (Rutherford, 1989, McCrea, 2008). Research findings predict that 23-90% of individuals experience at least one post-concussive symptom one month post-injury and about 40% have at least 3 symptoms at 3 months post-injury (Kibby & Long, 1996; Legome, Alt & Wu, 2009; Rimel, Giodarni, Barth, Boll & Jane, 1981; Russell & Smith, 1961; Rutherford, Merrett & McDonald, 1979). Patients who experience two or more symptoms at 3 months post-injury are likely to complain of a similar number 6-12 months post-injury and approximately two thirds of those who have PCS at 6 months post-injury display an increase in the number of symptoms between 6 weeks to 6 months post-injury (Alves, Colohan, O'Leary, Rimel & Jane, 1986; Kibby & Long, 1996; Rimel et al., 1981; Russell & Smith, 1961; Rutherford, 1989). There have been cases of some MTBI patients experiencing symptoms for up to 15 years (Rutherford, 1989).

Men suffer MTBI more frequently than women, however, the incidence of PCS is greater in females than in males (Bazarian, Blyth, Mookerjee, He & McDermott, 2009; McCauley, Boake, Levin, Contant, & Song, 2001; Ryan & Warden, 2003).

2.1 Clarifying Terminology and Criteria of PCS

Research in post-concussive symptoms (PCS) and post-concussive syndrome has presented researchers with challenges that range from differences in terminology to inconsistencies in criteria, affecting the definition and diagnosis of both transient PCS and persistent PCS. As such, the terminology of PCS has changed from its inception and varies between research groups. Post-concussive symptoms are often referred as post-*concussion* symptoms with PCS as an abbreviation for both. The meanings of both terms are essentially the same. However, some researchers use PCS to refer to post-concussive (concussion) *syndrome*. Syndrome refers to a pattern or collection of symptoms that persist beyond a certain period of time. Therefore, it is inappropriate to use PCS interchangeably to depict symptoms in some cases and syndrome in other cases. Even then, others identify persistent PCS as postconcussional disorder, postcontusional syndrome and posttraumatic syndrome (Boake et al., 2004; McCauley et al., 2001).

The 10th edition of the International Classification of Diseases (ICD-10) and the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) both propose persistent PCS criteria that are most cited in the PCS literature (American Psychological Association, 1994; World Health Organization, 1992). Figures 1 and 2 describe the ICD-10 and DSM-IV criteria respectively.

Figure 1: ICD-10 Diagnostic Criteria for Postconcussional Syndrome

A. History of head trauma with loss of consciousness precedes symptoms onset by maximum of four weeks
B. Symptoms in three or more of the following symptom categories: • Headache, dizziness, malaise, fatigue, noise tolerance • Irritability, depression, anxiety, emotional lability • Subjective concentration, memory, or intellectual difficulties without neuropsychological evidence of marked impairment • Insomnia • Reduced alcohol tolerance • Preoccupation with above symptoms and fear of brain damage with hypochondriacal concern and adoption of sick role
From "International Statistical Classification of Diseases and Related Health Problems", 10th ed, as cited in McCrea, 2008.

Figure 2: DSM-IV Research Criteria for Postconcussional Disorder

A. A history of head trauma that has caused significant cerebral concussion. Note: manifestations of concussion include loss of consciousness, posttraumatic amnesia, and, less, commonly, posttraumatic onset of seizures. The specific method of defining this criterion needs to be established by further research.
B. Evidence from neuropsychological testing or quantified cognitive assessment of difficulty in attention (concentrating, shifting focus of attention, performing simultaneous cognitive tasks) or memory (learning or recall of information).
C. Three (or more) of the following occur shortly after the trauma and last at least three months: 1. Becoming fatigued easily 2. Disordered sleep 3. Headache 4. Vertigo or dizziness 5. Irritability or aggression on little or no provocation

6. Anxiety, depression, or affective instability 7. Changes in personality (e.g., social or sexual inappropriateness) 8. Apathy or lack of spontaneity
D. The symptoms in criteria B and C have their onset following head trauma or else represent a substantial worsening of preexisting symptoms.
E. The disturbance causes significant impairment in social or occupational functioning and represents a significant decline from a previous level of functioning. In school-age children, the impairment may be manifested by a significant worsening in school or academic performance dating from the trauma.
F. The symptoms do not meet criteria for Dementia Due to Head Trauma and are not better accounted for by another mental disorder (e.g. Amnestic Disorder Due to Head Trauma, Personality Change Due to Head Trauma)
From the "Diagnostic and Statistical Manual of Mental Disorders, 4th ed., as cited in Ruff & Grant, 1999.

In ICD-10, the syndrome is described as symptoms in three or more categories that are present no later than four weeks post-injury, but this criteria requires a history of head injury "with a loss of consciousness". This is problematic as the MTBI literature shows that up to 90% of mild traumatic brain injury patients would be precluded from a formal diagnosis of persistent PCS because no loss of consciousness (LOC) was noted (McCrea, 2008). Similarly, in the DSM-IV diagnostic criteria, the LOC requirement will essentially render 90% of the MTBI patients non-eligible for a diagnosis of persistent PCS. The DSM-IV nosological system, in contrast to the ICD-10, requires that three or more symptoms last at least three months post-injury or substantial worsening of previously experienced symptoms post-injury to qualify for a diagnosis, together with a significant disruption to the daily life functioning of the individual (McCrea, 2008). At present, different symptom thresholds limit agreement between ICD-10 PCS and DSM-IV PCD; more specifically, DSM-IV PCD has a greater specificity compared to ICD-10 PCS (Boake et al., 2004). Therefore, due to the limitations in the existing diagnostic

criteria, clinicians are forced to improvise and select from alternative criteria that inherently allow inconsistent diagnostic decisions.

The disparity in terminology and references to PCS as well as the lack of consensus on the appropriate syndrome title further complicates the process of defining and diagnosing PCS. For the purpose of this thesis PCS refers to post-concussive symptoms, and persistent PCS (PPCS) refers to post-concussive syndrome.

2.2 Epidemiology of Persistent PCS

In view of the problems of classification, prevalence rates of persistent PCS are likely to be inaccurate because PCS studies naturally select only a subsample of the MTBI population, thus undermining the calculation of the true incidence of persistent PCS. Moreover, an estimated 25% of MTBI patients do not seek medical help post-injury and are not accounted for in the persistent PCS incidence (McCrea, 2008). In addition, most MTBI patients neither have LOC (an approximated 90%) nor long durations of post-traumatic amnesia (approximated 30-50%) in their acute injury characteristics which disqualifies them for a persistent PCS diagnosis under the DSM-IV or ICD-10 criteria.

Presently, published research estimates suggest that 15 to 20% of MTBI patients have persistent PCS beyond three months post-injury. However, when the problems of measuring true incidence are factored in, it appears that the approximation of PPCS is less than 5% of all MTBI patients (Iverson, 2005; Iverson, Zasler & Lange, 2006). Furthermore, it has been reported that the true incidence can drop to less than 1% of all MTBI patients depending on restrictions imposed by the diagnosis criteria (Iverson, 2005; Iverson, Zasler & Lange, 2006; McCrea, 2008).

2.3 Organic (Pathophysiological) Factors in PCS and PPCS

MTBI is associated with a range of pathological changes in the brain that are believed to be responsible for the clinical presentation of post-concussive symptoms (PCS) and persistent post-concussive symptoms (PPCS). Acceleration/deceleration forces or biomechanical forces occur when there is impact from a strike to the head by an object or a fall resulting in scalp injury, skull fracture, contusions, lacerations, hemorrhage and/or ischemia (Brown, Elovic, Kothari, Flanagan & Kwasnica, 2008; Gennarelli & Graham, 2005). Mild traumatic brain injury has traditionally been viewed as a form of 'diffuse axonal injury' (DAI) because acceleration/deceleration forces were believed to cause shearing or destruction of neurons leading to clinical symptoms (PCS) (Kibby & Long, 1996; Wasserman & Koenigsberg, 2007). The shearing forces cause disruption in the axonal functions and small vessels leading to localized transport failures, which amount to axon swelling and eventual neuronal cell death (Alexander, 1995).

In recent years, however, it appears that MTBI causes neuronal dysfunction but not destruction (Barr & McCrea, 2001). Neuronal dysfunction occurs due to ionic shifts, altered metabolism, impaired connectivity and changes in neurotransmission within the brain (Giza & Hovda, 2001). These sequential changes are collectively termed as the "neurometabolic cascade" (Giva & Hovda, 2001). Upon injury, sudden and spontaneous amounts of neurotransmitters are released and uncontrolled ionic fluxes occur. Excitatory transmitters bind to receptors causing neuronal depolarization, which results in an efflux of potassium ions and influx of calcium ions (Giza & Hovda, 2001; McCrea, 2008). The sodium-potassium pumps attempt to restore the neuronal homeostasis with an increase in adenosine triphosphate (ATP) resulting in a dramatic increase of glucose metabolism in the brain (Giza & Hovda, 2001). The hypermetabolic state occurs as a consequence of disparity between glucose supply/demand and

diminished cerebral blood flow, leading to a cellular energy crisis (McCrea, 2008). It is believed that in the state of energy crisis, the brain is susceptible to post-concussive vulnerability from which stem long lasting deficits. After the hypermetabolic state, the injured brain goes into a period of depressed metabolism.

Rat studies have shown that the neurometabolic processes return to normal by 7 to 10 days post-injury, however, in humans, metabolic depression can endure up to 4 weeks post-injury (Giza & Hovda, 2001). Notwithstanding, continual increases in calcium may cause impairment of the oxidative metabolism in the mitochondria and the exacerbation of the energy crisis. Increased calcium accumulation can trigger pathways leading to cell death. Intra-axonal calcium influx typically affects neurofilaments and microtubules damaging neural connectivity (Giza & Hovda, 2001; McCrea, 2008).

In summary, although there is sufficient evidence to show that a period of metabolic dysfunction follows MTBI with a return to normal brain metabolic function within several days or weeks post-injury depending on the severity of mild head injury, during which the manifestation of PCS occurs and usually ceases, the pathophysiology underlying MTBI and PCS cannot fully explain the persistence of PCS. Other non-organic factors must be considered to elucidate the etiology of PPCS.

2.4 Non-Organic Factors in PCS and PPCS

Research has revealed a host of other non-injury factors as being part of the etiology of PCS and PPCS, namely, demographic variables such as female gender and older age, medical complications such as comorbid medical or neurological disorders, severe associated injuries and previous head injury, psychosocial factors such as instability in relationships, absence of

social support network, preexisting psychiatric or personality disorder and substance abuse or dependency and lastly, situational concerns like litigation, compensation and post traumatic stress disorder (PTSD) (Alves et al., 1986; Bernstein, 1999; Carroll et al., 2004; Korinthenberg, Schreck, Weser & Lehmkuhl, 2004; McCrea, 2008; Mooney, Speed & Sheppard, 2005). In addition, post-concussive symptoms are highly non-specific in nature and bear resemblance to symptoms experienced after other kinds of injury, for example, orthopedic injury (McCrea, 2008).

2.5 Chapter Summary

There is a substantial increase in our understanding of problems surrounding PCS and PPCS. From a definition and diagnostic point of view, there remains much to be examined in establishing consistent terminologies and criteria. It also appears that the etiology of PCS is fraught with uncertainty regarding the contribution of organic (injury) and non-organic (non-injury) factors. The natural clinical course of MTBI has assisted in elucidating the probable causes of PCS and PPCS, that is, the initial manifestion of post-concussive symptoms may be related to neurometabolic changes in the brain which are organic in nature, however the persistence of symptoms may be caused by interplay between other non-injury factors such as psychological and psychosocial variables. At present, findings relating to non-organic factors are inconclusive. Functional outcome is strongly linked to the duration of PCS experienced and the interaction of the MTBI afflicted individual with the demands of daily life.

CHAPTER 3: INJURY AND NON-INJURY FACTORS IN PCS AND PPCS

The pathophysiology of MTBI shows that there is a clear neurological etiology for the acute symptoms and functional problems experienced in the first few days to weeks post-injury, however, in the case of PCS experienced outside of the conventional recovery time span, it appears that the condition cannot easily be accounted for by neurogenic (injury) factors.

Recently, studies pertaining to the injury factors have been inconclusive in establishing an association with PCS and raise the possibility that non-injury factors may make a greater contribution to post-concussive symptoms and the maintenance of persistent PCS (Begaz, Kyriacou, Segal & Bazarian, 2006; Binder, 1997; Huges et al., 2004). Furthermore, the non-specificity of PCS and subjectivity involved in understanding persistent PCS is further affected by motivational factors, especially when there is an impetus for financial or secondary gain (McCrea, 2008).

Notwithstanding the limitations introduced by the abovementioned issues, there are many studies in the literature that have found an association between psychological variables such as anxiety, depression and stress and PCS from three months post-injury and beyond (King, 1996). Preexisting psychiatric issues, psychological problems and certain personality types have been documented to impede recovery from MTBI and amplify the possibility of developing persistent PCS (Cattelani, Gugliotta, Maravita & Mazzucchi, 1996; Fenton, McClelland, Montgomery, MacFlynn & Rutherford, 1993; Greiffenstein & Baker, 2001; McCauley et al., 2001; Robertson, Rath, Fournet, Zelhart & Estes, 1994). It is also established that there is a connection between somatic conditions of chronic pain and sleep disturbance with persistent PCS (Fenton et al., 1993; Gouvier, Cubic, Jones, Brantley & Cutlip, 1992; Nicholson, 2000; Santa Maria, Pinkston, Miller & Gouvier, 2001).

Most studies examining factors implicated in the exacerbation of PCS and persistent PCS converge on a conclusion that persistent PCS is not solely a neurological or psychological condition, but a neuropsychological disorder, that is, while the neuropathophysiologic effects of MTBI initiate the process of PCS, the severity and maintenance of persistent PCS are the result of psychological, psychosocial and other non-MTBI specific factors (McCrea, 2008).

The following few sections will synthesize the evidence of injury and non-injury factors pertinent to the expression and maintenance of PCS. The injury factors or neurogenic factors comprise of MTBI severity which is determined by GCS, LOC and PTA, biochemical markers, type of injury, outcome from CT scan and MRI as well as trauma caused by the injury. The non-injury or psychogenic factors comprise of personality and psychological factors; namely, pre-existing personality types that may predispose one to PCS, anxiety, neuroticism, locus of control and depression. Furthermore, somatization as a demonstration of PCS, litigation/compensation and its possible motivational influence in the evolvement of persistent PCS will be evaluated.

3.1 Injury (Neurogenic) Factors/Indicators

3.1.1 Cognition, Neurocognitive and Neuropsychological Tests

Neurocognitive and neuropsychological tests have been utilized to measure the extent of change in cognitive status after an MTBI. While commonly reported symptoms in the acute stages post-injury entail slowed information processing abilities, memory problems and concentration difficulties, empirical support for such cognitive complaints in neuropsychological studies are less consistent (Alexander, 1995; Lundin et. al., 2006). Furthermore, a number of matched patient-control studies conducted in the acute stages of

MTBI have measured deficient performance on most objective tests used from different cognitive domains (Hugenholtz, Stuss, Stethem, & Richard, 1988; Levin et al., 1987; Macciocchi, Barth, Alves, Rimel, & Jane, 1996; Ponsford et. al., 2000; Voller et. al., 1996). The World Health Organization (WHO) Collaborating Centre Task Force on MTBI indicated that cognitive deficits and symptoms experienced by adults in the acute stages of MTBI generally resolve within three to twelve months (Carroll et. al., 2004). However, other meta-analyses show substantial cognitive recovery at around one month post-injury and near full recovery by the third month post-injury (Belanger, Curtiss, Lebowitz & Vanderploeq, 2005; Iverson, 2005; Schretlen & Shapiro, 2003). Well-controlled and methodologically sound studies examining the relationship between neuropsychological measures and the development and maintenance of PCS are limited. A study by Lidvall et al. (1974) revealed no significant differences on neuropsychological measures in MTBI patients with PCS. Jonsson et al. (1967) found only non-significant trends toward poorer performance on tests of perceptual speed in PCS patients as compared to controls. However, Leininger et al. reported that there were significant differences in reasoning, information processing and verbal learning in MTBI patients with persistent post-concussive symptoms (PPCS) compared to uninjured controls (1990). More recently, cognitive reserve capacity was implicated in the occurrence of post-concussive symptoms (PCS) following mild traumatic brain injury (Fay et al., 2010). Fay and colleagues conducted a prospective, longitudinal study in children who had sustained MTBI and children who had incurred orthopedic injuries and found that ratings of PCS were moderated jointly by cognitive ability and injury severity (2010). More specifically, children of lower cognitive ability with a complicated mild TBI were especially prone to cognitive symptoms across time and high acute levels of PCS, leading the authors to conclude that cognitive reserve is an important moderator of outcome post-MTBI in children and adolescents (Fay et al., 2010). However, such well-

designed studies are limited in an adult population and it is unknown whether similar findings will be elicited in adults. The relationship of cognition, neuropsychological and neurocognitive measures with the expression of PCS and PPCS is unclear and inconclusive.

3.1.2 MTBI Severity – GCS, LOC and PTA

GCS is necessary in the categorization of MTBI, however, it is not sensitive to detect subtle neurological changes or other physical and psychological post-concussive symptoms. The literature is inconclusive with regard to the role of PTA and LOC in the demonstration of PCS (Dikmen, Machamer, Winn & Temkin, 1995). Although it is reported that prolonged periods of unconsciousness or amnesia have a neuropsychological and functional impact following more severe TBI, the predictive capacity of these measures in MTBI is questionable (Dikmen et al., 1995). A brief LOC with a GCS of 13 to 15 is important, but not a critical indicator of post-concussive symptoms or functional outcome beyond the acute post-injury phase (Iverson, Lovell & Smith, 2000; Lovell, Iverson, Collins, McKeag, & Maroon, 1999). Likewise, PTA is less predictive of post-concussive symptoms beyond the pathophysiological changes in the acute post-injury phase of MTBI and is more applicable for severe forms of traumatic brain injury (McCrea, Kelly, Randolph, Cisler & Berger, 2002).

3.1.3 Biochemical Markers

Substantial research has focused on identifying biochemical markers that accurately classify an MTBI. The most promising of which are S-100 proteins, neuron-specific enolase (NSE) and cleaved tau protein (CTP) (McCrea, 2008). The S-100B neuroprotein is considered a

generally reliable marker for brain damage (Ingebrigtsen & Romner, 2002; Ingebrigtsen & Romner, 2003). S-100B is a calcium-binding protein found in high concentrations in astroglial and Schwann cells in the central nervous system. Upon cell damage, it is hypothesized that S-100B released into the cerebrospinal fluid (CSF) crosses the blood-CSF barrier (McCrea, 2008). Higher concentrations of S-100B have been reported in MTBI patients compared to controls (Mussack et al., 2002; de Kruijk, Leffers, Menheere, Meerhoff & Twijnstra, 2001). Despite the utility of these biochemical markers in identifying an MTBI, they are less applicable in determining PCS. Bazarian et al. studied the association of serum S-100B and CTP levels with long-term outcome after MTBI (2006). Only a weak correlation was found between marker levels and scores on the Rivermead Post-Concussion Symptoms questionnaire (S-100B, R = 0.071; CTP, R = 0.21) and correlation between acute marker levels and PCS after three months was not statistically significant (Bazarian, Blyth & Cimpello, 2006). Another review by Begaz et al. consisting of 11 studies assessing S-100B protein, NSE and CTP showed that none of the markers consistently predicted PCS (Begaz et al., 2006). It appears that considering clinical factors together with biochemical markers may be more appropriate in predicting PCS after MTBI (Begaz et al., 2006).

3.1.4 Type of Injury

Research pertaining to the type of MTBI injury and the severity of PCS is limited. A study by Ingebrigtsen et al. with a sample of 100 consecutive patients found no association between cause of injury and Rivermead Post-Concussion Symptoms questionnaire score three months after minor head injury (1998). In contrast, Ponsford et al. reported that patients who sustained an MTBI by motor vehicle accidents had more post-concussive symptoms and

persistent PCS at 1 week and 3 months post-injury respectively (2000). However, in their sample, the number of females who incurred an MTBI from a motor vehicle accident was higher than males and the authors attributed the increased frequency of symptom reporting to the higher proportion of females more so than type of injury (Ponsford et al., 2000). Although injury type and PCS severity has not been well researched thus far, the inconclusive results from available studies indicate that type/mode of injury does not reliably predict PCS.

3.1.5 Outcome from CT Scan and MRI

CT scans are used in hospitals to provide efficient triage and evaluate traumatic brain injury (McCrea, 2008). MRI scanning is a more sensitive neuroimaging method compared to CT scanning, but is considerably more expensive (McCrea, 2008). In United States, an estimated 3-10% of CT scans taken from TBI patients reveal brain abnormalities and less than 1% require neurosurgical intervention (National Centre for Health Statistics, 2003). The most common abnormalities after concussion on CT are cerebral contusions, subdural hematomas, epidural hematomas and edema (McCrea, 2008). Iverson and colleagues found that of 100 MTBI patients who underwent CT scans on the day of injury and then completed a small battery of neuropsychological tests within two weeks of injury, patients with complicated MTBI (with abnormalities in CT scan) performed significantly worse than patients with uncomplicated MTBI (without abnormalities in CT scan) on selected neuropsychological measures (2006). However, the effect sizes in the study were small or medium and the complicated and uncomplicated MTBI groups could not be differentiated in their eventual clinical outcome using logistic regression analysis (Iverson, Brooks, Collins & Lovell, 2006). A similar study by McCauley et al. demonstrated that patients with complicated MTBI were not associated with

increased risk for PCS three months post-injury (McCauley et al., 2001). Hughes et al. studied a series of 80 MTBI patients using MRI and neuropsychological testing during the acute injury phase followed by a PCS assessment at six months post-injury (2004). The investigators reported a weak correlation between MRI abnormalities and functional impairments on neuropsychological testing during the acute phase, but there was no significant correlation between MRI abnormalities and eventual PCS (Hughes et al., 2004).

3.1.6 MTBI-related Trauma or PTSD

Sustaining an MTBI is often a traumatic experience regardless of the mode of accident. Post-traumatic stress disorder (PTSD) is characterized by the re-experiencing of an extremely traumatic event, usually by way of nightmares and intrusive thoughts of the incident (American Psychiatric Association, 2000). Studies have shown that compared to MTBI patients without PTSD, MTBI patients with PTSD were significantly more depressed and anxious (Moore, Terryberry-Spohr & Hope, 2006). Furthermore, many who suffer PTSD post-injury continue to experience symptoms for several months or even years (Moore et al., 2006). Levin et al. reported that 13% of MTBI patients in a sample of 60 showed prevalence of PTSD and 18% met the criteria for comorbid depression (2001). Research also shows that patients who report PCS such as fatigue, dizziness, headache and pain experience significantly greater PTSD symptoms compared to those who do not despite having similarities in head injury severity (Feinstein, Hershkop, Jardine & Ouchterloney, 2000). Harvey and Bryant found that increasing age, a history of PTSD, depression score and an avoidant coping style increased an individual's risk for developing acute symptoms of a stress response, a pre-cursor to PTSD (1998). Another study by Bryant et al. investigated the relationship between post-concussive symptoms and

PTSD in an MTBI population where survivors of motor vehicle accidents who sustained an MTBI (n = 46) were compared to those who did not sustain a traumatic brain injury (n = 59) six months post-trauma for PTSD and PCS (1999). Post-concussive symptoms were more evident in MTBI patients with PTSD than those without PTSD and post-concussive symptoms were significantly correlated with PTSD (Bryant & Harvey, 1999). Research examining the presence of PTSD with LOC and PTA is inconclusive. Studies argue that LOC and PTA are protective mechanisms that shield the individual from the development of PTSD after MTBI (Mayou, Bryant & Duthie, 1993; Sbordone & Liter, 1995). However, others suggest that PTSD can exist in the absence of an overt memory for a traumatic event and emotional reactions to trauma can be retained without conscious recall through 'pseudomemories', which are analogous to the flashbacks experienced in PTSD in MTBI patients with LOC and PTA (Bryant, 1996). The findings demonstrate that trauma from MTBI plays a significant role in the manifestation of PCS through the mediation of both neurological and psychological factors.

3.2 Non-Injury (Psychogenic) Factors

3.2.1 Pre-Existing Personality Types

Certain personality types may predispose patients to prolonged PCS. Through the characterisation of clinical cases, Kay, Newman, Cavallo, Ezrachi and Resnick (1992), and Ruff, Camenzuli and Mueller (1996) have described the following personality types which are likely to be vulnerable to PCS:

- the overachiever, characterised by obsessive-compulsive behaviour and drivenness, is prone to catastrophic thinking when he/she finds difficulty in meeting daily demands

- the dependent person is debilitated by his/her symptoms and is unable to cope independently causing a perpetuating vicious cycle of learned-helplessness
- the insecure person shares some similarities with the dependent person, but has a tendency to dwell and focus on self-doubt, resulting in a magnification of his/her symptoms
- the grandiose person fails to acknowledge that he/she is functioning at a less than optimum level and takes on tasks that result in failure causing a crash to his/her self-esteem
- the person with borderline personality characteristics who has difficulty relating to others is the most suceptible to personality disorganization in all forms after an MTBI

It is proposed that these personality types coupled with the emotional salience of the accident may trigger old, unresolved emotional issues which usually evince as feelings of being unprotected and ignored when sick or hurt. People who have significant shortcomings in their emotional nurturing are most at risk for PCS after an MTBI (Kay et al., 1992).

3.2.2 Anxiety

There is substantial evidence in the literature to suggest that the relationship between MTBI and anxiety is birectional, that is MTBI plays a role in the emergence and expression of anxiety; and anxiety potentially affects the prognosis and recovery of a person afflicted with MTBI (Moore et al., 2006). However, the interaction between anxiety and PCS remain unclear. In addition, to further obscure the boundaries of classification, symptoms experienced in PCS largely overlap with symptoms of anxiety.

Location of injury in the brain may play a contributory role to the anxiety sequelae following MTBI as associations have been found in the right orbital cortex, occipital lobe and

temporal injuries with the regulation of anxiety (Epstein & Ursano, 1994). Anxiety is more common in left hemisphere damage compared to right hemisphere damage and manifests as over-sensitivity, excessive cautiousness and exaggerated appraisal of one's impairments (Epstein & Ursano, 1994). Exhibiting indifference and a lack of insight are commonly seen as part of right hemisphere damage (Epstein & Ursano, 1994).

It is widely acknowledged that many individuals who have sustained a MTBI experience highly stressful and possibly life-altering events that are both short-term such as hospitalization or long-term such as the eventual realization of a possible permanent impairment (Moore et al., 2006). These stressors can evolve to either become post-traumatic stress disorder (PTSD) or sometimes unleash a pre-existing psychiatric condition (Harvey, Brewin, Jones & Kopelman, 2003). In fact, psychiatric history has a significant association with MTBI (Epstein & Ursano, 1994). Group profiles for cases of persistent PCS demonstrate highest levels on the Hysteria, Hypochondriasis and Depression scales of the MMPI (Youngjohn, Burrows, & Erdal, 1995). Furthermore, MTBI is known to break down psychological defenses and previously effective coping strategies, leaving one vulnerable to the relapse of previously experienced anxiety conditions (Moore et al., 2006).

3.2.3 Neuroticism

Neuroticism is considered as a personality trait in psychology. It is a disposition to approach happenings in one's life with negativity, that is, people who have greater neuroticism have a higher tendency than the average to experience feelings of anxiety, anger, guilt and clinical depression (Matthews & Deary, 1998). Neuroticism is believed to be a predisposition

for the development of anxiety-related problems such as phobia and generalized anxiety disorder (Hettema, Prescott & Kendler, 2004; Matthews & Deary, 1998).

Neuroticism has not been investigated in detail with regard to PCS and PPCS. Keshavan et al. (1981) found that in a sample of 60 head-injury admissions of varying severity, pre-morbid neuroticism score derived from relatives' accounts was significantly associated with PCS reporting rate at three months post-injury. Lishman (1988) also acknowleged that neuroticism is influential in the emergence of persistent PCS. However, the relationship between neuroticism and PCS is inconclusive; some studies have shown that people who have greater scores on neuroticism scales are more predisposed to PCS, however, others have failed to find a significant association between the two variables (Anstey, Butterworth, Jorm, Christensen & Windsor, 2004; Freeman, 2000).

3.2.4 Locus Of Control

Locus of control refers to the extent to which individuals believe that they can control events that affect them. Individuals with a high internal locus of control believe that events result primarily from their own behavior and actions whereas those with a high external locus of control believe that powerful others, fate, or chance primarily determine events (Rotter, 1990). Kay et al. (1992) noted differences in early responses to symptoms based on internal evaluations. The manner in which one internally discerns their cognitive and physical symptoms, that is, either magnifying or minimizing them, given that the objective evaluation of their symptoms is constant results in the difference between an external behaviour of either passivity (for example, recuperating in bed) or resilience (for example, attempting to live life just as it was prior to the injury regardless of the symptoms).

Locus of control assumes the role of a catalyst in PCS demonstration where the manifestation of symptoms undergo an internal evaluation based on the personality characteristics of the individual.

3.2.5 Depression

Contrary to the more definitive and established results found in the anxiety literature, the number of studies investigating depression and depressive personality is scant. For example, Cicerone and Kalmar (1997) examined the contribution of premorbid affective disturbance to persistent PCS between two case-matched groups of patients with and without a history of pre-injury depression. No significant differences on self-reported PCS and MMPI scales were found. They concluded that caution needs to be exercised in attributing PCS to the presence of pre-morbid depression.

In contrast, a review by Busch and Alpern (1998) found that despite methodological differences in the criteria used across studies, there was a concomitance rate of at least 35% that left frontal damage was associated with depression following MTBI. A trend showed that depression can possibly continue for many years after MTBI and the authors postulated that MTBI may be a triggering event for a set of pathophysiological changes, as well as, a corresponding depressive episode in a vulnerable subset of the population. Schoenhuber and Gentilini (1988) followed up 35 patients and matched-controls between 5 to 17 months post-injury with the Self Rating Depression Scale and the State-Trait Anxiety Inventory. Patients were found to be at risk for developing depression, but not anxiety post-MTBI and concluded that all MTBI patients should be screened for depression.

Although depression caused by PCS and clinical depression may share the same underlying substrates, the dearth of research in the area of PCS-related depression leaves much more to be investigated.

3.2.6 Somatisation in PCS

Somatoform disorders involve the self-report of physical symptoms that are more attributable to psychological than organic causes (Gasquoine, 1997). They differ from factitious disorders and malingering in that the symptom production is involuntary although the distinction is purely theoretical as there is no known way of delineating whether symptom production is voluntary or involuntary (Binder, 1990, McCrea, 2008). In a study by Lishman (1968), soldiers with penetrating head injuries from World War II were evaluated retrospectively to explore symptoms in relation to several indices of brain damage and of 670 soldiers with penetrating head injuries, 144 showed significant psychiatric disability one to five years later. Furthermore, in 71 of the soldiers, complaints consisted of persistent headache, dizziness, fatigue or sensitivity to noise and when compared to the remainder of soldiers, had milder head injuries as measured by the depth of penetration, amount of brain tissue destroyed and length of PTA as well as less intellectual impairment. This study corroborates the notion that organic aetiology cannot completely account for the persistence of PCS reported by the soldiers and implicates non-organic factors.

3.2.7 Litigation and Compensation

Litigation and compensation complicate the symptom reporting of PCS. In a meta-analytic review of 18 studies including 2,353 individuals with varying severity of TBI, the effect of financial incentive on outcome after incurring a head injury was relatively significant (effect size = 0.47) and constituted about 20-25% of persistent symptom reporting after TBI (Binder & Rohling, 1996). Feinstein et al. prospectively studied the role of litigation on PCS in 97 consecutive individuals 6 weeks post-injury and established that patients involved in litigation reported significantly more anxiety and social dysfunction and had poorer outcomes in the Glasgow Coma Scale and the Rivermead Head Injury Follow-up Questionnaire than patients not involved in litigation (2001).

Yet, on the other end of the spectrum, some studies report that litigation and compensation have no association with the frequency or severity of PCS (Keshavan, Channabasavanna & Reddy, 1981; Rimel et al., 1981). In addition, Fenton et al. (1993) stated that the "litigation neurosis", a term coined by Millar in 1961, has been largely refuted in the PCS literature. Given the stressful and hostile nature of litigation and compensation proceedings, it is perceived that some level of psychosocial functioning and symptom presentation will inevitably be affected (McAllister & Arciniegas, 2002).

3.3 Chapter Summary

Currently, studies investigating both injury (neurogenic) and non-injury (psychogenic) factors in the emergence and maintenance of PCS face theoretical and methodological challenges. Nonetheless, it is clear that neurogenic factors are less predictive of PCS and persistent PCS than psychogenic factors. Within injury factors, neurocognitive tests,

MTBI severity, injury type, biochemical markers as well as CT and MRI scanning appear to contribute less to the understanding of PCS than MTBI-related trauma. There is greater consistency in PTSD studies suggesting that psychological factors, compared to neurological factors, assume the role of mediating variables in the manifestation of PCS. Within non-injury factors, the most conclusive evidence points to anxiety being crucial in the demonstration of PCS. Research has not scrutinized other personality and psychological factors as thoroughly, however, the relationship of anxiety to other personality factors presents evidence that there exists a complex interaction between such factors and PCS manifestation.

CHAPTER 4: RATIONALE AND STUDY AIMS

Common findings in the literature relating to PCS suggest that both injury factors including MTBI-related trauma or PTSD and non-injury factors including personality traits, particularly dispositions to anxiety and stress are aspects in determining the presence, severity and longevity of post-concussive symptoms. However, more consistent evidence suggests that anxiety in particular plays an important role in the manifestation of PCS. Presently, the relative contributions of anxiety-related personality and psychological factors remain unspecified (Moore et al., 2006). Furthermore, the role of anxiety disposition and its relationship with PCS is yet to be studied extensively in an Asian population. Therefore, the present study has the following aims:

1. Investigate the effects of injury (neurogenic), personality (dispositional/trait) and psychological (state) factors in people who have recently incurred a mild traumatic brain injury (MTBI) compared with healthy controls.
2. Determine the differences in injury (neurogenic), personality (dispositional/trait) and psychological (state) factors and the relationship between these factors in relation to severity of post-concussive symptoms in people who have recently sustained a mild traumatic brain injury (MTBI).
3. Explore the pattern of differences in injury, personality and psychological factors in relation to severity of post-concussive symptoms (PCS) at 3 months and 6 months after baseline assessment.
4. Examine the differences in injury, personality, and psychological factors in MTBI patients with persistent post-concussive symptoms (PPCS) and MTBI patients who have recovered from post-concussive symptoms (PCS).

5. Determine the best predictor of post-concussive symptoms in this sample.

CHAPTER 5: METHODOLOGY

5.1 Research Participants

65 mild traumatic brain injury patients and 58 controls were recruited for the study over the course of one and a half years. After removal of some participants due to incomplete data collection and missing data, the final sample consisted of 62 patients and 51 controls. Of the 62 patients, 33 were males and 29 were females and of the 51 controls, 27 were males and 24 were females.

5.2 Inclusion and Exclusion Criteria

Patients were deemed appropriate for the study if they met the following inclusion criteria which details a GCS score of between 13 to 15 at admission, no LOC or LOC of under 30 minutes, no PTA or PTA of less than 60 minutes, between the ages 18 to 70 years, able to speak and write English, no pre-existing neurological illness such as epilepsy, stroke, dementia, multiple sclerosis (MS), or any other neurological condition, and no significant visual, hearing or language impairments. The patients were excluded if they met the following criteria which entails a PTA of greater than 60 minutes, a LOC of more than 30 minutes, a history of neurological disease and/or ongoing substance abuse as defined as usage of illegal drugs and significant alcohol use characterized by more than 10 standard drinks a week.

5.3 Procedure

5.3.1 Intake Interview

Patients who fit the study criteria were identified for recruitment and referred by consulting neurosurgeons and registrars on the day of their outpatient appointment at the Mild Head Injury Clinic, National Neuroscience Institute, TanTock Seng Hospital, Singapore. The outpatient appointment was given as a follow-up from their initial admission to the accident and emergency department after sustaining an MTBI. Medical records were also screened to ensure eligibility for the study. The study protocol was then explained in detail to referred patients followed by an opportunity to ask questions. Subsequently, consent to participate in the study was obtained. Patients who were below twenty-one years of age were required to obtain consent from their parent or guardian. Patients were asked to make an appointment in the following week on a suitable day and time of their convenience for their baseline assessment.

Control participants were recruited through advertisements posted around the National University of Singapore (NUS) campus and mainly comprised of the auxilliary staff from NUS. Interested participants were given an appointment to be seen for the assessment in one of the psychology laboratories at NUS. The study protocol was explained in detail and they had an opportunity to clarify any doubts. After which, signed consent was obtained for their participation and participants who were below the legal age of twenty-one were required to obtain parental or guardian consent.

5.3.2 Baseline Assessment

The baseline assessment for patients was conducted at the Neuroscience clinics in the National Neuroscience Institute (NNI). During the assessment, information regarding the

patient's current head injury and medical history as measured by the Philadelphia Head Injury Questionnaire (PHIQ) (Curry, Ivins & Gowen, 1991), trauma evaluation as measured by the Impact of Events Scale (IES) (Horowitz, Wilner & Alvarez, 1979) and symptoms severity as measured by the Rivermead Post-Concussion Symptoms Questionnaire (RPQ) (King, Crawford, Wenden, Moss & Wade, 1995), as well as, clinical and demographic history as assessed by a self-constructed questionnaire (see appendix 1) were enquired in detail. After which, a series of neuropsychological tests assessing attention, memory, speed of processing and executive functioning were conducted to assess cognitive status. Personality measures tapping on the five facets of personality (neuroticism, extraversion, openness to experience, agreeableness and conscientiousness) as assessed by the NEO Five Factor Inventory (NEO-FFI) (Costa & McCrae, 1985), state and trait anxiety as measured by the State-Trait Anxiety Inventory (STAI) (Spielberger, Gorusch, Lushene, Vagg, & Jacobs, 1983), depression as measured by the Beck Depression Inventory II (BDI-II) (Beck, Steer & Brown, 1996) and locus of control as assessed by the Rotter's Locus of Control Scale (Rotter, 1966) were also administered. A test assessing malingering (Test of Memory Malingering – TOMM) (Tombaugh, 1996) was included in the battery. Patients who failed to meet threshold scores in the malingering test were excluded from the study at the baseline assessment. The assessment lasted for about two hours and the test protocol was counterbalanced. Patients were compensated with S$40 upon the successful completion of the assessment. Mandarin versions of tests acquired from respective test distributors or widely used in the Singapore clinical services were used for patients who were only literate in Mandarin. The Singapore clinical services have reliably translated commonly used neuropsychological tests for their practice. In the event where the Mandarin translation was unavailable, the English version of the assessment was translated with permission of the test publishers. All Singapore and permanent residents are required to go through mandatory

primary education. As such even though patients may claim not be literate in English, they do have basic conversational English skills. Moreover, care was taken to recruit suitable patients who would be able to handle the battery of tests.

For the controls, after consent was obtained, they were screened for prior psychiatric problems, previous head injury episodes and medical complications using the PHIQ and the self-constructed questionnaire. Those who had no complications such as stroke, history of siezures, severe depression, learning disability and substance use disorder were included in the study and administered the rest of the neuropsychological test battery except for the assessments and portions of measures related to current head injury status. They were also compensated with S$40. The controls were only seen at one time point, that is, at the baseline assessment.

5.3.3 3-month Follow-up Assessment

The same battery comprising of standardized tests and questionnaires measuring cognitive, psychological and social domains, personality and demographics was administered to patients approximately three months after their baseline assessment. Again, patients were seen in the neuroscience clinic at NNI and the assessment lasted for about one and a half hours. The purpose of neurocognitive assessment in this study was to provide a more comprehensive and complete profile of the changes in cognition in the MTBI sample being assessed. A compensation of S$40 was given to patients for successfully completing the follow-up assessment.

5.3.4 6-month Follow-up Phone Call

Patients were called approximately six months after their baseline assessment for their final assessment over the telephone where three questionnaires were administered, that is, the Rivermead Post-Concussion Symptoms Questionnaire (RPQ), State-Trait Anxiety Inventory (STAI) and the Beck Depression Inventory II (BDI-II). Patients were informed in advance through a text message and/or a phone call that they should expect a phone call on a particular date and time and were requested to have a pen and paper ready for answering the questionnaires. They were advised that the phone call would take about fifteen to twenty minutes. For the RPQ and the STAI, patients were required to write down the answering scheme and reply accordingly when the questions were asked. For the BDI-II, they had to listen and respond to the questions asked by the assessor. At the end of the assessment, if patients requested for a consultation with a psychologist, further advice was given pertaining to their next course of action.

5.4 Measures Administered

5.4.1 Injury-Related and Clinical History Assessment Tests

Head injury status and recovery were assessed by the Philadelphia Head Injury Questionnaire (PHIQ) (Curry et al., 1991) and the Rivermead Post-Concussion Symptoms Questionnaire (RPQ) (King et al., 1995). The PHIQ is a structured information gathering instrument consisting of both objective and subjective questions pertaining to personal and medical history, as well as, physical, cognitive and personality changes after MTBI (Koch, Merz & Lynch, 1995). Patients primarily respond to the questions with either ‘Yes’ or ‘No’ and are asked for clarifications when necessary. The RPQ is a standardised self-administered tool

that determines the presence and severity of PCS experienced after MTBI by comparing perceived functioning before the MTBI with over the past 24 hours. Patients are required to rate 0 (no experience of symptoms) to 4 (severe experience of symptoms) on a likert scale for each of the 17 symptoms stemming from somatic, cognitive and psychological domains. In addition, the Impact of Events Scale (IES) (Horowitz et al., 1979) which encompasses 15 items, each caliberated on a 4-point likert scale ranging from 'Not At All' to 'Often' experienced, assessing potential post-traumatic stress incurred after MTBI was also measured to acquire a more complete clinical profile of the patients. A self-constructed demographic questionnaire detailing previous head injury occurence, problems related to psychological health, psychiatric history, drinking habits, educational level and occupation was also administered. The control participants were only administered the personal and medical history portion of the PHIQ, and the self-constructed demographic questionniare.

5.4.2 Injury-Related Assessment Tests: Neurocognitive Battery

The neurocognitive battery comprised of several standardised non-invasive tests that were carefully selected to assess broad cognitive domains such as attention, verbal memory, visual memory, working memory, speed of processing and executive functioning. The neurocognitive tests used in the study were categorised according to the aforementioned domains based on previous meta-analytical studies and the relevant literature on cognitive assessment (Binder, Rohling & Larrabee, 1997; Frencham, Fox & Maybery, 2005; Strauss, Sherman & Spreen, 2006). Attention and speed of processing were assessed by the written version of the Symbol Digit Modalities Test (SDMT) (Smith, 1991), which is commonly used to assess divided attention, visual scanning, tracking as well as motor speed and the Trails

Making Test A and B (Reitan, 1958) that measures attention, speed and mental flexibility. The Symbol Digit Modalities Test (SDMT) is extremely sensitive to brain insults in adults and children and is one of the most commonly used tests in TBI (Strauss, Sherman & Spreen, 2006). Significant group differences have been found on the SDMT between individuals with TBI and controls, and the task differentiates between individuals who are early versus late in the recovery process (Bate, Mathias & Crawford, 2001). SDMT also has utility in assessing persistent post concussive symptoms (Chan, 2001; Chan, Hoosain & Lee, 2003). The Trails Making Test (TMT) is sensitive to closed head injury in that TMT completion times increase with the severity of head injury (Dikmen et al., 1995). However, it has poor sensitivity which indicates that there is less utility in ruling out PCS, but also has high specificity which implies that there is greater utility in ruling in PCS, that is, persons without PCS are unlikely to have impaired scores. In addition, the predictive power of the speed score was strong establishing the diagnostic utility of the test (Cicerone & Azulay, 2002). It was also found that a patient at least three months after injury with impaired performance on the TMT A is about three times more likely to exhibit PCS than a person with intact performance on this measure (Cicerone & Azulay, 2002). Working memory was measured by both Digit Span and Spatial S pan from WMS-III (Weschler, 1997). Impairments in working memory constitute a core component of the cognitive deficits associated with traumatic brain injury (Mcallister, Flashman, Sparling & Saykin, 2004). Digit Span and Spatial Span are established measures with sound psychometric properties that assess working memory (Strauss, Sherman & Spreen, 2006). Verbal memory was determined by the total number of words remembered from the first five trials of the Rey Auditory Verbal Learning Test (RAVLT) and the RAVLT delayed recall trial (Strauss et al., 2006) as well as the Singapore adapted version of the Wechsler Memory Scales (WMS) Story Recall (Weschler, 1997) which assesses both immediate recall and delayed recall. The RAVLT

is sensitive to impairments in verbal memory in closed head injury patients (Shum, Harris & O'Gorman, 2000). Adults with closed head injury show improvement over repeated trials in the RAVLT and show both recency and primacy effects (Bigler, Rosa, Schultz, Hall & Harris, 1989). In addition, WMS Story Recall has been established as a sensitive test to assess difficulties in verbal memory as a result of traumatic brain injury (Fisher, Ledbetter, Cohen, Marmor & Tulsky, 2000). To assess visual memory, the Continuous Visual Memory Test (CVMT) (Trahan & Larrabee, 1988) that comprises both the total score as measured by accurately recognizing and distinguishing between targets (7 figures that are repeated periodically in a stack of 112 cards) and distractors across 96 trials and the delayed recognition score as measured by the ascertainment of the target from 6 other figures were used. The CVMT has been documented to be one of the more sensitive measures of visual memory deficits in mild head injury patients (Handbook of psychological assessment By Gérald Goldstein, Michel Hersen, 2000). For the assessment of executive functioning, the Verbal Fluency (animals) (Strauss et al., 2006), which evaluates the spontaneous production of words under restricted search conditions and the Victoria Stroop test (Strauss et. al., 2006), which assesses the ease at which an individual can maintain a goal in mind and suppress a habitual response in favour of a less familiar one were utilized. For the Stroop which has three conditions, that is, the dot condition, the word condition and the colours condition, the interference score that is measured by the subtraction of the time taken for the dot condition from the time taken for the colours condition (time taken for colours condition – time taken for dots condition) is indicative of performance level. A smaller time difference is representive of better performance. There is considerable evidence that the frontal lobes are particularly vulnerable in traumatic brain injury and because executive processes rely on intact frontal structures, verbal fluency tests, which heavily involve the frontal regions, are sensitive measures to reveal executive dysfunction

(Levin & Kraus, 1994). A validated mandarin equivalent was obtained and used for mandarin-only literate participants (Lee, 2003; Lee, 2003a). Head-injured patients typically perform slower on all of the sub-tests within Stroop (Batchelor, Harvery & Bryant, 1995). Finally, the Test of Memory Malingering (TOMM) (Tombaugh, 1996) was included in the battery of assessments to ensure that patients and controls were not exaggerating or faking cognitive symptoms. Table 1 summarizes all the questionnaires, scales and neurocognitive tests used in the study.

5.4.3 Personality and Psychological Assessment Questionnaires

The personality component of the battery of assessments consisted of the State-Trait Anxiety Inventory (STAI) for adults (Spielberger et al., 1983), the Beck Depression Inventory II (BDI-II) (Beck et al., 1996), the NEO Five-Factor Inventory (NEO-FFI) (Costa & McCrae, 1985) and Rotter's Locus of Control Scale (Rotter, 1966). The STAI is a self-report questionnaire categorized into 'state' and 'trait' anxiety with 20 items each, graded on a 4-point likert scale. 'State' anxiety is the anxiety experienced in a temporary condition or situation and 'trait' anxiety is the general level of anxiety one experiences, which is considered to be more enduring and stable. High scores indicate high anxiety levels. The BDI-II measures the severity of self-reported depression in a 21-question scale with 4 options scored from 0 to 3. Higher scores are reflective of more severe depressive symptoms. The NEO-FFI is a 60-item, shortened version of the NEO Personality Inventory and consists of five domains; neuroticism, extraversion, openness to experience, agreeableness and conscientiousness with 12 items in each domain measured on a 5-point likert scale ranging from 'Strongly Disagree' to 'Strongly Agree'. The Rotter's Locus of Control Scale comprises of 23 'Yes' or 'No' forced-choice questions deciphering whether one has an internal locus of control or an external locus of

control. The score exists on a continuum, with a higher score depicting a more external locus of control and a lower score indicating a more internal locus of control.

Table 1: Questionnaires, scales and cognitive tests administered in the study

Injury-related/Clinical History details	Personality Assessments	Cognitive Battery
Philadelphia Head Injury Questionnaire (PHIQ)	State-Trait Anxiety Inventory (STAI)	Symbol Digit Modalities Test (SDMT) Trails Making Test
Rivermead Post-Concussion Symptoms Questionnaire (RPQ)	Beck Depression Inventory II (BDI-II)	Digit span Spatial span
Self-Constructed Demographic Questionnaire	NEO Five Factor Inventory (NEO-FFI)	Rey Auditory Verbal Learning Test (RAVLT) WMS Story Recall
Impact of Events Scale (IES)	Rotter's Locus of Control Scale	Continuous Verbal Memory Test Victoria STROOP Verbal Fluency (Animals) Test of Memory Malingering (TOMM)

5.5 Data Analysis

Data analysis was performed using SPSS version 16.0. The alpha level for all statistical analyses was set at .05 unless otherwise specified. Independent t-tests were used to determine no significant differences in age and level of education between the patient group and control group. The sample profile of the population and injury profile of the patients were obtained through descriptive statistics. Assumptions for parametric testing were met. The data was normally distributed. Following that, univariate and multivariate analyses were used to compare patients and controls at the baseline assessment for neurogenic factors that comprised of the

neurocognitive battery of tests and psychogenic factors that consisted of tests from personality (STAI (trait anxiety), locus of control, neuroticism in the NEO-FFI) and psychological domains (STAI (state anxiety) and BDI-II). This was conducted to see the emerging personality profile of patients versus the controls. Post-hoc analysis was done in the manner of t-tests or Tukey when deemed necessary and relevant. When multiple testing was involved, significant levels were adjusted according to the Bonferroni correction to account for increased type 1 error.

One-way analysis of variance and multivariate tests were used to assess differences across PCS severity groups at the baseline assessment. Appropriate post-hoc tests were then conducted with Bonferroni correction to alpha. Repeated measures mixed ANOVAs were conducted to assess any changes in performance in the neurocognitive tests, personality and psychological measures across PCS severity between baseline, 3-month follow-up and 6-month follow-up assessments with Bonferroni correction to the p-value. Independent t-tests and odds ratio analyses were performed on both neurogenic (injury) factors and psychogenic (personality/psychological) factors to profile persistent PCS and recovered PCS groups. Correlation analysis was performed with the data at baseline assessment firstly amongst the injury factors with PCS score and secondly among personality/psychological variables with PCS score to examine the strength of association among variables and as a precursor to regression analyses. Regression analyses were executed on the patient group to find the best predictor of PCS.

CHAPTER 6: RESULTS

6.1 Demographic And Injury Details Of Patients And Controls

6.1.1 Age and Education

65 MTBI patients and 58 controls were recruited for the study. For the MTBI patients, out of the recruited number, 1 was suspected to be malingering (TOMM score = <45) and 2 had extensive missing data. As a result, they were excluded from the sample. For the controls, 7 had either extensive missing data or did not pass the screening test for being considered suitable for the study and were excluded from the sample. Therefore, the final sample consisted of 62 MTBI patients and 51 healthy controls. This finalized sample consisted of 33 males and 29 females for MTBI patients and 27 males and 24 females for the healthy controls. For both age and education level as measured by number of years, independent t-tests confirmed that there were no significant differences between patients and controls. Furthermore, independent t-tests also confirmed that there were no significant differences for age and education level for gender within each of the groups. A summary of age and education details for patients and controls is provided in table 2.

Table 2: Details on age and education for patients and controls

Participants	N	Age = Years		Education = Years	
		M	*SD*	*M*	*SD*
Patients	62	34.84	15.00	11.79	3.19
Controls	51	37.82	15.99	12.19	3.80
Male Patients	33	30.88	13.85	12.12	3.03
Male Controls	27	32.78	17.19	13.57	2.65
Female Patients	29	39.34	15.24	11.41	3.38
Female Controls	24	43.50	12.59	10.64	4.32

6.1.2 Race and Occupation

The study sample contained participants from 3 main ethnic groups, that is, Chinese, Indians and Malays, and some foreign participants working in Singapore (see figure 3). The distribution of occupation for the study sample is shown in figure 4.

Figure 3: Race distribution of patients and controls

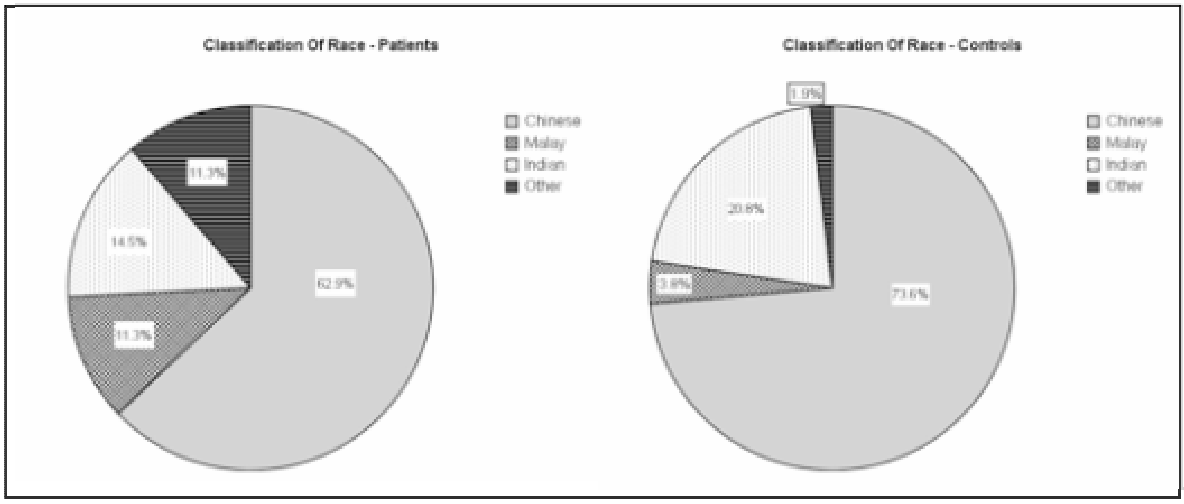
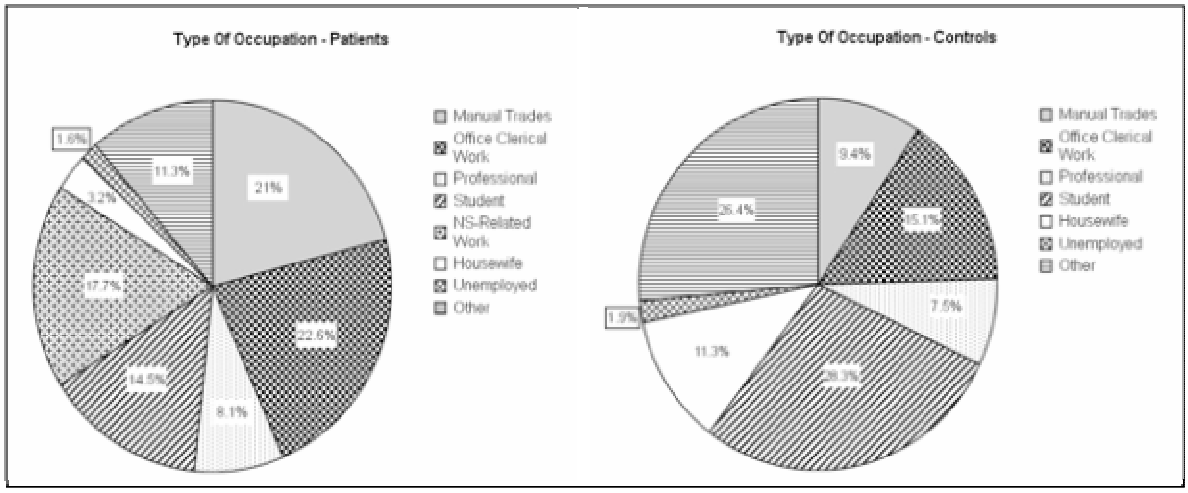


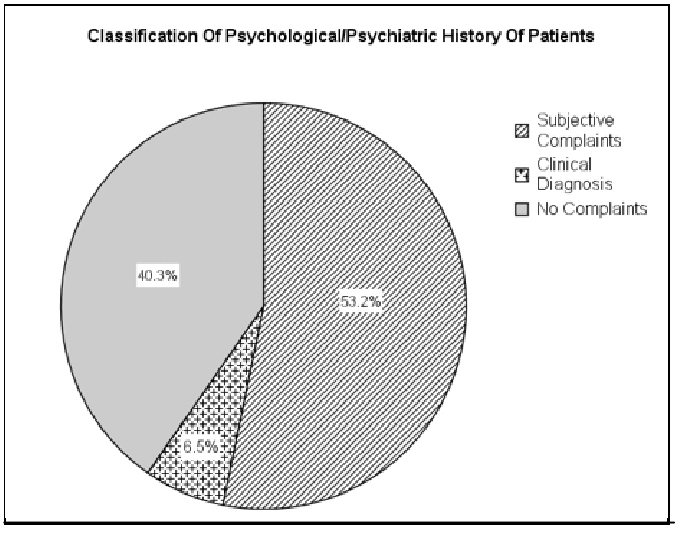
Figure 4: Occupation distribution of patients and controls



6.1.3 Psychiatric History and Injury Details

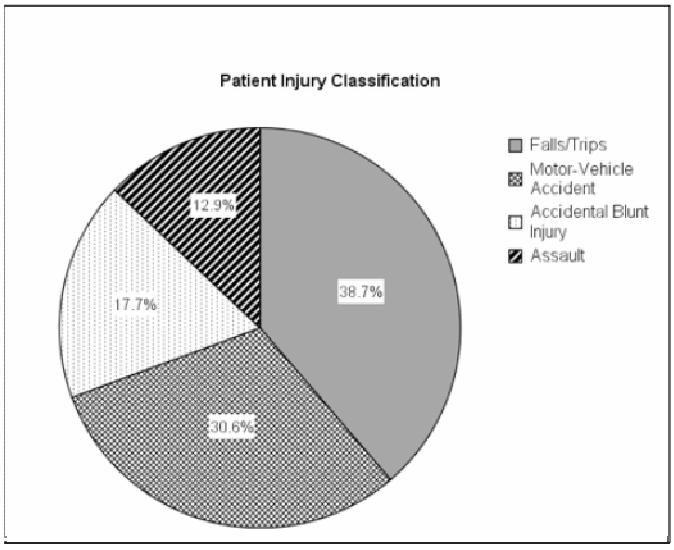
Patients filled in a demographic questionnaire to endorse whether they felt the following symptoms at any time in their lives: depression/low mood, anxiety, hearing voices in their heads that talked to them or ordered them to do things, seeing things that other people cannot see or had complaints of pain in parts of their body that cannot be accounted for by physical injury. These were taken to be subjective complaints. If the patient had a diagnosis given by a psychiatrist, they were deemed to have a prior psychiatric history. Figure 5 shows the distribution of psychiatric and psychological history in the MTBI patient sample of this study. Controls were selected such that they had no clinical or subjective complaints.

Figure 5: Distribution of psychiatric/psychological history of patients



Most of the MTBI patient sample incurred their injuries from falls or tripping. Figure 6 pictorially represents the injury distribution.

Figure 6: Injury distribution of patients



95.2% of the patient sample had clear CT scans. Scalp haematomas were also considered to be in the clear category as injury was external and not to the brain. 4.8% of the patients were found to have intracranial bleeding that was not treated, but were considered to resolve with time. These cases still fell within the criteria for a mild traumatic brain injury. The mean GCS score for patients was 14.98 (*SD* = 0.13). All patients had a GCS score of 15 except one who had a GCS of 14. None of the patients had stroke or seizures, but 29% had a previous head injury. Similarly, none of the controls had stroke or seizures, but 4.4% had incurred a previous head injury. 60.9% of the MTBI patients were seeking compensation or litigating their injury.

Finally, the mean time in days from MTBI injury was measured by the date of admittance into the emergency department to the baseline assessment. Thereafter, the mean time

was calculated between the baseline assessment and 3-month follow-up and 6-month follow-up. Table 3 shows the collated information on injury characteristics and mean time between the injury occurrence and assessments.

Table 3: Injury characteristics and mean time from injury and assessments

Variables	M	SD	%
GCS Score	14.98	0.13	-
CT Scan	-	-	95.2 (clear) 4.8 (intracranial bleed)
Previous Head Injury			29 (Yes)
Stroke			100 (No)
Seizures			100 (No)
Time from MTBI to baseline assessment (Days)	50.46	42.03	-
Time from baseline assessment to 3-month follow-up (Days)	93.23	8.32	-
Time from 3-month follow-up to 6-month follow-up (Days)	89.13	11.26	-

Therefore, the baseline assessment was conducted approximately two months post-injury; the 3-month follow-up was approximately five months post-injury; and the 6-month follow-up was approximately eight months post-injury.

6.2 Comparison of MTBI Patients and Controls: Baseline Assessment at Two Months Post-Injury

6.2.1 Injury/Neurogenic Factors: Neurocognitive Tests

Multivariate and univariate analysis of variance showed no significant differences between patients and controls for the neurocognitive tests at baseline assessment (see table 4). There were no gender effects. No significant interaction effects were found.

Table 4: Means, SDs and F-test results for neurocognitive tests at baseline assessment two months post-injury

Measures	MTBI Patients (n = 62) *M* (*SD*)	Controls (n = 51) *M* (*SD*)	*F*	*p* (2-tailed)
Attention/ Speed			**2.458**	**.067**
Symbol digits modalities test	49.23 (13.77)	54.57 (10.49)	-[a]	-
Trail making test A (time in secs)	29.43 (12.36)	24.43 (8.68)	-	-
Trail making test B (time in secs)	66.21 (33.77)	58.87 (19.35)	-	-
Working memory			**0.917**	**.403**
WMS-III Digit span total	17.69 (4.44)	18.40 (3.75)	-	-
WMS-III Spatial span total	16.23 (3.80)	17.08 (3.47)	-	-
Verbal memory			**1.412**	**.217**
RAVLT (5 trials total)	52.75 (12.49)	54.57 (11.80)	-	-
RAVLT (delayed recall)	29.00 (1.75)	29.04 (1.22)	-	-
Story A (immediate recall)	8.31 (2.82)	8.66 (2.82)	-	-
Story A (delayed recall)	6.95 (2.78)	7.55 (2.98)	-	-
Story B (immediate recall)	9.20 (2.25)	8.66 (2.95)	-	-
Story B (delayed recall)	8.22 (2.72)	8.45 (3.26)	-	-
Visual memory				
CVMT (Total Score)	71.68 (12.13)	72.83 (8.75)	0.239	.626
CVMT (Delayed Recognition Score)	4.33 (1.68)	4.21 (1.87)	0.208	.649
Executive functioning			**0.751**	**.474**
STROOP (interference score – time in secs)	12.47 (8.63)	10.92 (7.01)	-	-
Category Verbal Fluency (animals)	20.68 (6.08)	20.42 (5.33)	-	-

Group differences are tested with multivariate (*F* and *p* values in bold) and univariate analysis of variance.
[a]Further univariate analyses are performed only when MANOVAs are significant.
* $p<.05$, ** $p<.01$.

6.2.2 Personality (Dispositional/Trait) Factors: Trait Anxiety, Neuroticism and Locus of Control

A two-way analysis of variance revealed significant main effects for group in trait anxiety, neuroticism and locus of control. Patients scored higher than controls in all of the aforementioned personality domains (see table 5). No significant gender differences were obtained in the personality measures. There was a significant group by gender interaction effect for trait anxiety only, which was attributable to male patients having significantly higher trait anxiety scores (M = 47.15, SD = 12.69) as compared to male controls (M = 35.64, SD = 6.14), $t(48) = -4.61$, $p = .001$ (see figure 7).

Figure 7: Interaction effect for trait anxiety at baseline assessment

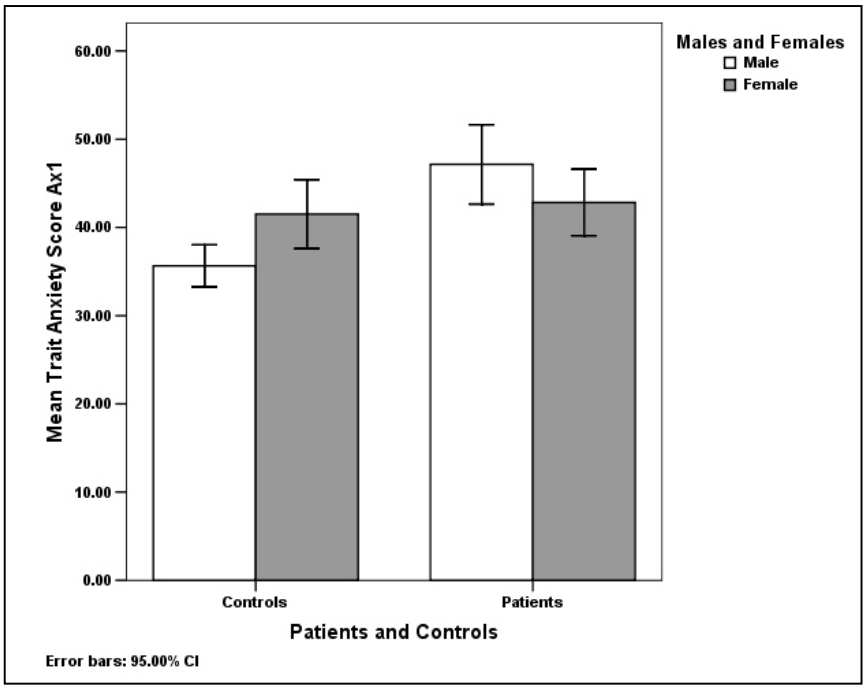


Table 5: Means, SDs and F-test results for personality/psychological measures at baseline assessment two months post-injury

Measures	Personality Domains	MTBI Patients (n = 62) *M* (*SD*)	Controls (n = 51) *M* (*SD*)	*F*	*p* (2-tailed)	Effect Size[a] (Cohen's *d*)
STAI	Trait Anxiety	45.13 (11.58)	38.35 (8.21)	11.71	.001**	0.65
NEO-FFI	Neuroticism	54.74 (10.92)	48.82 (8.88)	9.21	.003**	0.58
Rotter's Locus of Control Scale	Locus of Control	13.65 (3.69)	11.25 (4.30)	9.02	.003**	0.58
STAI	State Anxiety	38.00 (11.75)	31.16 (7.97)	11.66	.001**	0.65
BDI-II	Depression	13.29 (12.07)	6.44 (7.87)	11.86	.001**	0.65

[a]Effect sizes are calculated based on Thalheimer & Cook (2002).
Group differences are tested with univariate analysis of variance.
* $p<.05$, ** $p<.01$.

6.2.3 Psychological (State) Factors: State Anxiety and Depression

A two-way analysis of variance revealed significant main effects for group in state anxiety and depression. Patients scored higher than controls in the aforementioned psychological domains (see table 5). No significant gender differences were obtained in the personality measures. There were no interaction effects.

6.3 Comparison by PCS Severity: Baseline Assessment at Two Months Post-injury

6.3.1 Injury/Neurogenic Factors: Neurocognitive Tests

Multivariate analysis of variance and one-way analysis of variance did not yield any significant differences among PCS classification groups for the majority of the cognitive tests except for the total score of the CVMT in the visual memory domain, $F(2, 59) = 3.56$, $p = .04$, $d = 0.74$ (see table 6). However, post-hoc comparisons failed to reach significance.

Table 6: Means, SDs and F-test results for neurocognitive tests at baseline assessment two months post-injury according to PCS Classification

Measures	No Symptoms (n = 14) *M* (*SD*)	Mild Symptoms (n = 27) *M* (*SD*)	Moderate-severe Symptoms (n = 21) *M* (*SD*)	*F*	*p* (2-tailed)
Attention/ Speed				**0.396**	**.880**
Symbol digits modalities test	49.23 (14.52)	49.59 (15.30)	48.76 (11.75)	-[a]	-
Trail making test A (time in secs)	27.00 (9.87)	28.41 (12.89)	32.24 (13.05)	-	-
Trail making test B (time in secs)	60.23 (26.39)	64.41 (28.51)	72.24 (43.36)	-	-
Working memory				**0.924**	**.452**
WMS-III Digit span total	18.15 (4.54)	17.89 (4.56)	17.18 (4.39)	-	-
WMS-III Spatial span total	16.23 (3.79)	15.56 (3.40)	17.05 (4.25)	-	-
Verbal memory				**0.653**	**.792**
RAVLT (5 trials total)	48.38 (13.08)	53.64 (10.87)	54.38 (13.86)	-	-
RAVLT (delayed recall)	28.23 (2.89)	29.28 (0.89)	29.05 (1.56)	-	-
Story A (immediate recall)	7.77 (3.11)	8.96 (2.62)	7.86 (2.83)	-	-
Story A (delayed recall)	6.08 (2.53)	7.56 (2.89)	6.76 (2.76)	-	-
Story B (immediate recall)	8.85 (3.00)	9.48 (1.69)	9.10 (2.39)	-	-
Story B (delayed recall)	7.62 (2.79)	8.80 (2.58)	7.90 (2.84)	-	-
Visual memory					
CVMT (Total Score)	75.00 (7.68)	74.41 (8.27)	66.36 (16.23)	3.555	.035*
CVMT (Delayed Recognition Score	4.62 (1.57)	4.48 (1.74)	3.95 (1.69)	0822	.444
Executive functioning				**0.242**	**.914**
STROOP (interference score – time in secs)	11.54 (6.08)	13.26 (10.30)	12.04 (7.90)	-	-
Category Verbal Fluency (animals)	20.54 (6.57)	21.11 (6.13)	20.23 (5.98)	-	-

Group differences are tested with multivariate (*F* and *p* values in bold) and univariate analysis of variance.
[a]Further univariate analyses are performed only when MANOVAs are significant.
* $p<.05$, ** $p<.01$.

6.3.2 Personality (Dispositional/Trait) Factors: Trait Anxiety, Neuroticism and Locus of Control

One-way analysis of variance was used to delineate differences in the personality measures among MTBI patients according to PCS classification. Patients were categorized into 'no symptoms', 'mild symptoms' and 'moderate-severe symptoms' groups in accordance with the number and severity of symptoms endorsed in the Rivermead PCS Questionnaire at the baseline assessment. The Rivermead PCS questionnaire consists of a likert scale for the measure of severity with 0 indicating 'Not experienced at all', 1 indicating 'No more of a problem', 2 indicating 'A mild problem', 3 indicating "A moderate problem' and 4 'A severe problem', of 17 commonly experienced post-concussive symptoms. King and colleagues advised that total PCS score equates to the sum of all symptom scores excluding the ratings of 1 and 0 (1995). For the purposes of this study, scores were further categorized into ranges such as 0-1 to signify 'no symptoms', 2-22 to indicate 'mild symptoms' and 23-68 to denote 'moderate-severe symptoms'. This categorization was an extrapolation based on the aforementioned suggestion of King and colleagues on how to use the RPQ scale. The 'No symptoms' group was aptly allocated a score of 1 or less as a symptom rating of 2 on any one of the symptom would imply a mild problem. The maximum score possible on the scale was 68 and it was divided into three to obtain the upper threshold of the 'mild symptoms' category. Anything above that was classified as moderate to severe symptoms. This classification was therefore logical. The categorization of symptoms into these groups presents a basis for comparison of patients varying in symptom severity in a systematic and organized manner, which was necessary to prove the hypotheses of the study.

Trait anxiety score differed significantly across the 3 PCS classification groups, $F(2, 59) = 4.23$, $p = .02$, $d = 0.89$. Post-hoc testing for trait anxiety using Tukey HSD showed a significant difference in comparison between the 'no symptoms' and the 'moderate-severe symptoms' groups with latter group ($M = 50.50$, 95% CI [45.35, 55.65]) demonstrating higher trait anxiety scores than the 'no symptoms' group ($M = 40.69$, 95% CI [34.89, 46.49]), $p = .04$.

Significant group differences across PCS classification were not found for neuroticism and locus of control scores.

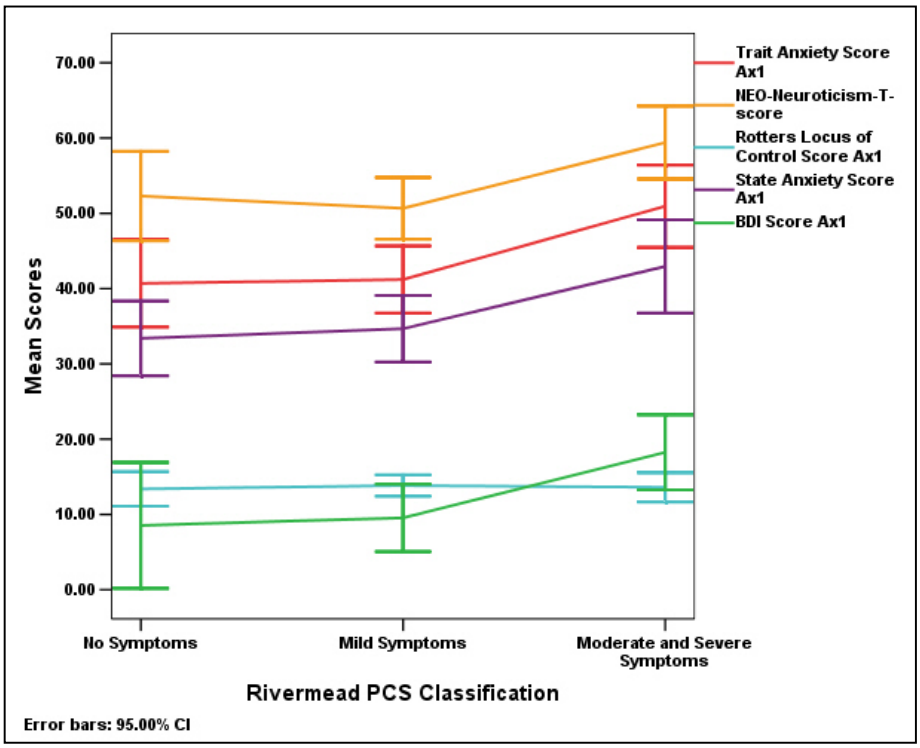
6.3.3 Psychological (State) Factors: State Anxiety and Depression

State anxiety score differed significantly across the 3 PCS classification groups, $F(2, 59) = 3.44$, $p = .04$, $d = 0.84$. However, Tukey HSD post-hoc tests were not significant.

Depression score also differed significantly across the 3 PCS classification groups, $F(2, 59) = 4.96$, $p = .01$, $d = 0.95$. Tukey HSD post-hoc analysis of the 3 groups indicated significant differences in the comparison of the 'moderate-severe symptoms' group with the 'no symptoms' group and the 'mild symptoms' group. The 'moderate-severe symptoms' group ($M = 19.32$, 95% CI [14.53, 24.10]) had significantly higher depression scores than the 'no symptoms' group ($M = 8.54$, 95% CI [0.18, 16.90]), $p = .02$ and the 'mild symptoms' group ($M = 10.67$, 95% CI [6.51, 14.82]), $p = .03$.

Figure 8 shows the distribution of mean scores at 95% confidence intervals for both the personality (dispositional/trait) and psychological (state) measures.

Figure 8: Distribution of mean scores on personality and psychological measures across PCS classification



6.3.4 Litigation

An independent t-test was conducted on PCS scores of patients based on their litigation status at two months, five months and eight months post-injury. There were no significant differences in PCS scores between those who were seeking compensation through litigation and those who were not at all three time points. Similar non-significant results were obtained for neuroticism, depression, state and trait anxiety at all three time points.

6.4 Comparison By PCS Severity – Long-Term Outcome

A total of 53 (85.4%) patients returned for their 3-month follow-up assessment. The 3-month follow-up assessment was conducted approximately five months post-injury. 9 (14.5%) patients were not assessed as they were not contactable and 1 (1.6%) withdrew from the study. For the 6-month follow-up assessment, which was conducted approximately eight months post-injury, 44 (71.0%) patients participated. 17 (27.4%) patients were not assessed as they were not contactable and 1 (1.6%) withdrew from the study. T-tests showed no significant differences in age and education between patients who failed to return for follow-ups and those who remained in the study. Significance for multiple post-hoc comparisons was set at the Bonferroni corrected alpha level of .017.

6.4.1 Injury/Neurogenic Factors: Neurocognitive Tests

Most of the cognitive tests failed to yield significant differences between the baseline assessment at two months post-injury and the 3-month follow-up assessment at five months post-injury through the repeated measures mixed design ANOVA. However, some tests from the attention/speed, visual memory and verbal memory domains showed significant differences from time 1 to time 2. Paired t-test post-hoc comparisons revealed that these were attributable to the 'no symptoms', 'mild symptoms' and/or 'moderate-severe symptoms' groups depending on the tests. There were no significant main effects for Rivermead PCS classification across all tests. Interaction effects were observed portraying an opposite trend compared to the other groups in the 'mild symptoms' group in tests from the verbal memory and working memory domains. Table 7 shows the tests

with a significant main effect for time. Table 8 shows the significant paired t-tests for post-hoc analysis. Figures 9 and 10 show the significant interaction effects from the 2 tests in the verbal memory and working memory domains respectively.

Table 7: Cognitive tests with significant main effect for time between baseline assessment at two months post-injury and 3-month assessment at five months post-injury across PCS classification

Measures	Time 1 – Baseline Assessment			Time 2 – 3-month Follow-up			*F*	*p* (2-tailed)
	No Symptoms (n = 9) *M* (*SD*)	Mild Symptoms (n = 23) *M* (*SD*)	Moderate-Severe Symptoms (n= 21) *M* (*SD*)	No Symptoms (n = 9) *M* (*SD*)	Mild Symptoms (n = 23) *M* (*SD*)	Moderate-Severe Symptoms (n = 21) *M* (*SD*)		
Attention/ Speed Symbol digits modalities test	44.13 (11.36)	52.48 (14.27)	46.29 (12.91)	49.25 (11.89)	53.65 (11.98)	50.52(12.18)	8.10	.006*
Verbal memory RAVLT (5 trials total)	48.75 (14.27)	53.87 (11.25)	53.57 (13.64)	55.38 (13.02)	61.78 (10.94)	59.24 (7.99)	24.48	.001**
Story A (immediate recall)	7.25 (2.66)	9.13 (2.62)	7.57 (2.91)	8.88 (2.10)	9.48 (2.61)	9.24 (2.59)	11.56	.001**
Story A (delayed recall)	5.13 (1.73)	7.78 (2.84)	6.60 (2.72)	7.38 (2.62)	8.48 (3.09)	8.45 (2.50)	17.61	.001**
Visual memory CVMT (Total Score)	74.75 (8.99)	74.92 (8.36)	66.05 (16.56)	80.13 (9.57)	81.00 (8.62)	76.10 (14.49)	11.80	.001**
CVMT (Delayed Recognition Score)	4.50 (1.77)	4.63 (1.74)	4.00 (1.72)	5.75 (1.28)	5.54 (1.22)	5.10 (1.74)	27.08	.001**

* $p<.05$, ** $p<.01$.

Table 8: Significant post-hoc analysis results for cognitive tests between baseline assessment at two months post-injury and 3-month assessment at five months post-injury across PCS classification

Measures	No Symptoms (n = 9)	Mild Symptoms (n = 23)	Moderate-Severe Symptoms (n = 21)	No Symptoms		Mild Symptoms		Moderate-Severe Symptoms (n = 21)	
	M (*SD*) at baseline vs. *M* (*SD*) at 3-month follow-up			*t*-value	*p* (2-tailed)	*t*-value	*p* (2-tailed)	*t*-value	*p* (2-tailed)
Attention/ Speed Symbol digits modalities test	44.13 (11.36) vs. 49.25 (11.89)		46.29 (12.91) vs. 50.52 (12.18)	-2.67	.032*			-2.39	.027*
Verbal memory RAVLT (5 trials total)	48.75 (14.27) vs. 55.38 (13.02)	53.87 (11.25) vs. 61.78 (10.94)	53.57 (13.64) vs. 59.24 (7.99)	-2.85	.025*	-7.13	.001**	-2.17	.042*
Story A (immediate recall)			7.57 (2.91) vs. 9.24 (2.59)					-3.28	.004*
Story A (delayed recall)			6.60 (2.72) vs. 8.45 (2.50)					-3.49	.002*
Visual memory CVMT (Total Score)	74.75 (8.99) vs. 80.13 (9.57)	74.92 (8.36) vs. 81.00 (8.62)	66.05 (16.56) vs. 77.10 (14.49)	-3.09	.018*	-4.74	.001**	-2.29	.033*
CVMT (Delayed Recognition Score)	4.50 (1.77) vs. 5.75 (1.28)	4.63 (1.74) vs. 5.54 (1.22)	4.00 (1.72) vs. 5.10 (1.74)	-3.42	.011*	-3.70	.001**	-3.10	.006**

* $p<.05$, ** $p<.01$.

Figure 9: Interaction effect due to ‘mild symptoms’ group in Story B – Delayed Recall Test

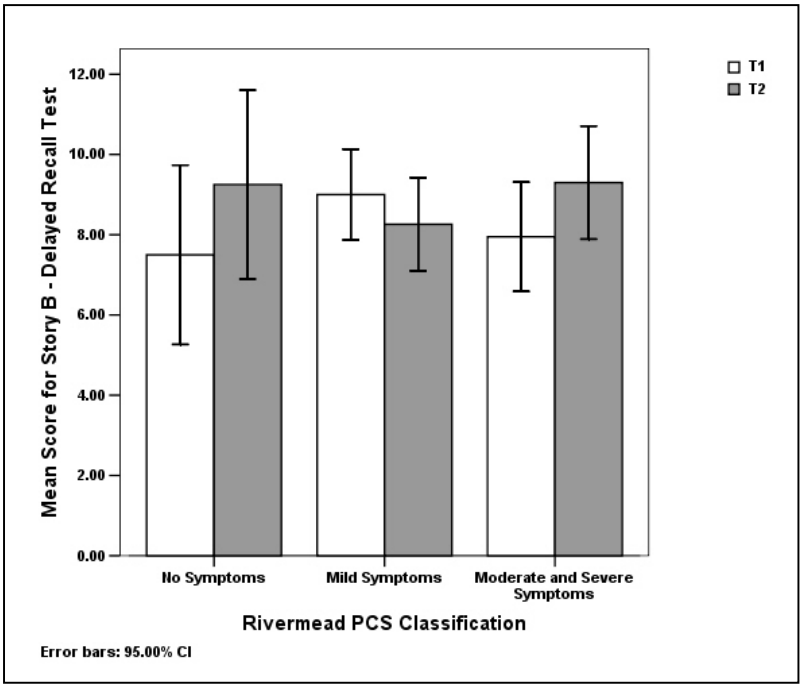
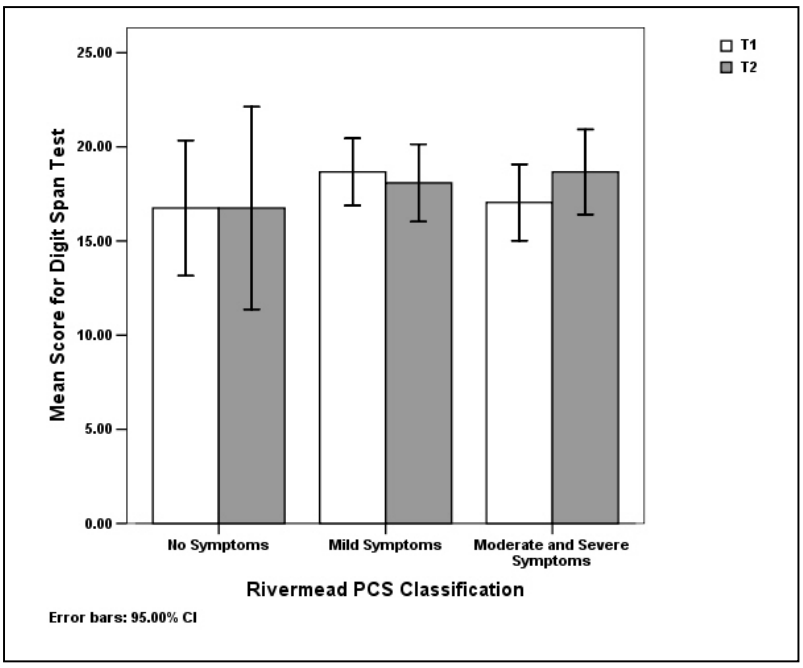


Figure 10: Interaction effect due to ‘mild symptoms’ group in Digit Span Test



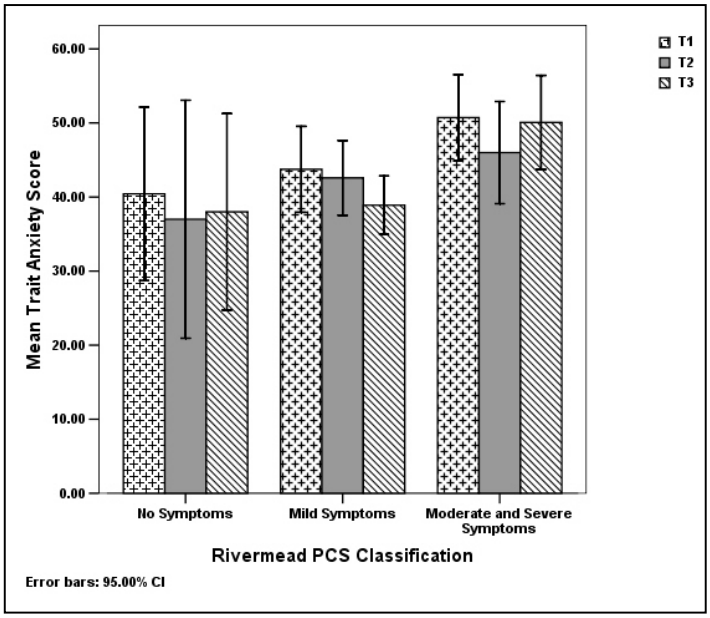
6.4.2 Personality (Dispositional/Trait) Factors: Trait Anxiety and Locus of Control

A repeated measures mixed-ANOVA design was executed to examine the pattern of changes in the tests assessing personality among the baseline, 3-month follow-up and 6-month follow-up assessments at two months, five months and eight months post-injury respectively. The Bonferroni correction was applied to the alpha level before interpreting the results.

For trait anxiety, as expected, there was neither a significant main effect for time nor a significant interaction effect across the three time points. However, there was a significant main effect for PCS classification group, $F(1, 37) = 3.33$, $MSE = 291.80$, $p = .047$. Post-hoc analysis failed to show any significant differences between the groups but there was a strong trend (permissible to be reported as per Winer, Brown & Michels (1970)) for the 'moderate-severe symptoms' group having a higher trait anxiety score compared to the 'no symptoms' group, $p = .07$. Figure 11 shows the relationship between trait anxiety scores at the three time points and PCS classification.

There were no significant effects for time and PCS classification groups for locus of control scores across time 1 and 2. There were also no interaction effects.

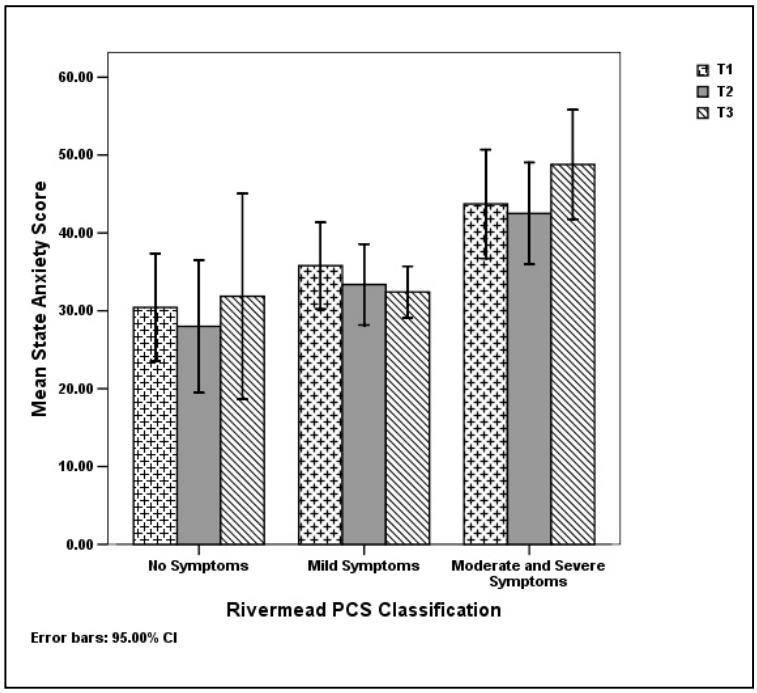
Figure 11: Relationship of trait anxiety scores at 3 time points with PCS classification



6.4.3 Psychological (State) Factors: State Anxiety and Depression

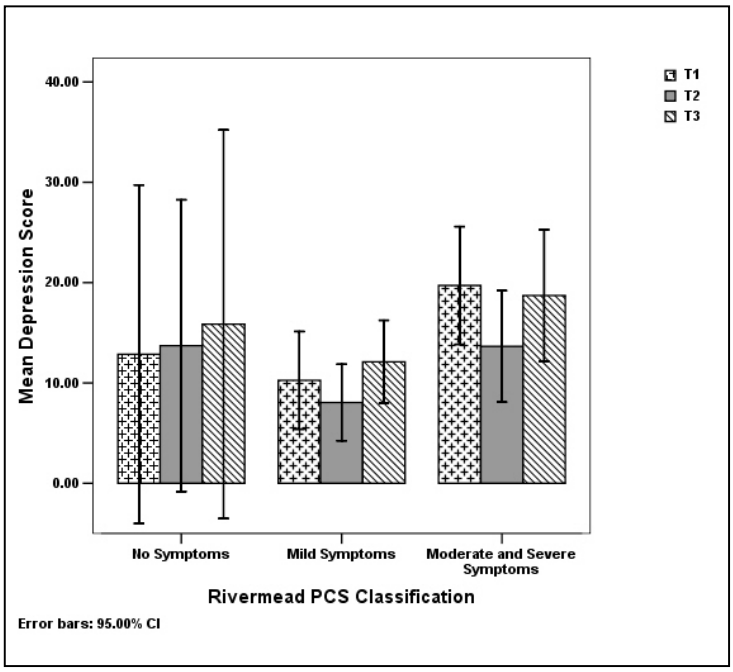
There was neither a significant effect for time nor a significant interaction effect for state anxiety across the three time points. However, there was a significant main effect for PCS classification group, $F(2, 37) = 9.16$, $MSE = 232.04$, $p = .001$ and post-hoc analysis revealed that the 'moderate-severe symptoms' group, ($M = 45.00$, 95% CI [40.24, 49.76]), continued to have significantly higher state anxiety score than the 'no symptoms' group, ($M = 30.10$, 95% CI [23.36, 36.83]), $p = .002$ and the 'mild symptoms' group, ($M = 33.86$, 95% CI [29.77, 37.95]), $p = .03$. Figure 12 shows the relationship between state anxiety scores at the three time points and PCS classification.

Figure 12: Relationship of state anxiety scores at 3 time points with PCS classification



The main effect of time was significant for depression scores, $F(2, 74) = 4.03$, $MSE = 30.52$, $p = .02$, indicating a significant difference in average depression scores across the three time points independent of PCS classification of patients. Paired t-tests revealed that there was a significant difference between the 3-month follow-up and 6-month follow-up assessments, $t(13) = -4.35$, $p = .001$, for the 'moderate-severe symptoms' group at the Bonferroni corrected alpha level of .017. There were no significant effects for PCS classification and no interaction effects between time and PCS classification group membership. Figure 13 shows the relationship between depression scores at the three time points and PCS classification. There appears to be a large variation in scores caused by high patient attrition within the 'no symptoms' group.

Figure 13: Relationship of depression scores at 3 time points with PCS classification



6.5 Persistent PCS (PPCS) versus Recovered PCS

Patients were reclassified into those with persistent PCS and recovered PCS according to their Rivermead PCS total scores at the 3-month follow-up assessment, that is, five months post-injury. Only patients who returned at five months post-injury were included in the analysis (total: n = 57, persistent PCS: n = 34, recovered PCS: n = 23). The time from injury to the 3-month follow-up assessment was greater than 144 days, which was sufficient time passed to warrant persistent PCS classification according to the definition of persistent PCS, that is, 3 or more symptoms lasting beyond 3 months. An endorsement of 'mild problem' for any 3 symptoms in the Rivermead PCS Questionnaire was taken to be the minimum threshold for the classification of persistent PCS.

There were no significant differences between persistent PCS (PPCS) and recovered PCS groups in age and education level. A series of independent t-tests and odds ratio analyses were conducted where appropriate to compare and examine the respective effects of injury factors such as scores on neurocognitive tests, GCS, LOC, type of injury, CT scan, previous head injury and MTBI-related trauma or PTSD as measured by the Impact of Events Scale (IES), and non-injury factors such as the scores on personality (dispositional/trait) and psychological (state) measures. MTBI-related trauma or PTSD was also assessed for differences at the 3-month follow-up assessment to see whether residual traumatic effects lasted longer in PPCS patients.

6.5.1 Injury/Neurogenic Factors: Neurocognitive Tests

Independent samples t-tests for the neurocognitive tests showed significant differences between the PPCS and recovered PCS groups for the total score of the CVMT in the visual memory domain and Category Verbal Fluency test in the executive functioning domain. The remainder of the tests showed no significant differences between groups (see table 9).

Table 9: Means, SDs, t-test results and effect sizes for neurocognitive measures based on baseline assessment two months post-injury

Measures	Persistent PCS Patients (n = 34) *M* (*SD*)	Recovered PCS Patients (n = 23) *M* (*SD*)	*t*-value	*p* (2-tailed)	Effect size[a] (Cohen's *d*)
Attention/ Speed					
Symbol digits modalities test	46.97 (12.85)	54.22 (14.71)	1.92	.06	-
Trail making test A (time in secs)	30.88 (13.35)	25.17 (8.77)	-1.80	.08	-
Trail making test B (time in secs)	70.39 (36.69)	53.83 (22.20)	-1.93	.06	-
Working memory					
WMS-III Digit span total	17.62 (4.42)	18.48 (4.41)	0.72	.47	-
WMS-III Spatial span total	16.26 (4.11)	16.65 (3.55)	0.37	.71	-
Verbal memory					
RAVLT (5 trials total)	51.42 (12.65)	55.17 (12.39)	1.10	.28	-
RAVLT (delayed recall)	28.79 (2.16)	29.30 (0.97)	1.21	.23	-
Story A (immediate recall)	7.82 (3.14)	8.91 (2.23)	1.53	.13	-
Story A (delayed recall)	6.82 (2.74)	7.17 (2.87)	0.47	.64	-
Story B (immediate recall)	9.09 (2.47)	9.26 (1.96)	0.28	.78	-
Story B (delayed recall)	8.15 (3.00)	8.22 (2.37)	0.09	.93	-
Visual memory					
CVMT (Total Score)	68.76 (13.93)	75.74 (8.83)	2.13	.04*	0.58
CVMT (Delayed Recognition Score)	4.15 (1.82)	4.65 (1.50)	1.09	.27	-
Executive functioning					
STROOP (interference score – time in secs)	12.76 (8.07)	10.57 (7.42)	-1.04	.30	-
Verbal Fluency (animals)	19.38 (5.76)	23.13 (6.23)	2.33	.02*	0.64

[a]Effect sizes are calculated based on Thalheimer & Cook (2002).

* $p < .05$, ** $p < .01$.

6.5.2 Injury/Neurogenic Factors: GCS, LOC, Injury Type and Trauma

Independent t-test showed no significant differences between persistent PCS and recovered PCS groups in GCS score and MTBI-related trauma as assessed by the total score on the IES and its two subscales (Avoidance Scale and Intrusion Scale) at baseline assessment. Odds ratio analyses indicated no significant differences between the groups for LOC, previous head injury and type of injury such as falls/trips, motor vehicle accidents and accidental blunt injury, but showed that the PPCS group was significantly more prone to experiencing assaults (odds ratio = 4.75) and having unclear CT scans (odds ratio = 7.77) compared to the recovered PCS group.

At five months post-injury, independent t-tests indicated significant differences for MTBI-related trauma. PPCS patients scored significantly higher on the IES total score (PPCS: M = 23.77, SD = 20.57 vs. recovered PCS: M = 9.00, SD = 9.15; $t(45) = -3.50$, $p = .001$), Avoidance Scale score (PPCS: M = 12.90, SD = 11.73 vs. recovered PCS: M = 5.80, SD = 6.97; $t(49) = -2.71$, $p = .009$) and Intrusion Scale score (PPCS: M = 10.90, SD = 9.93 vs. recovered PCS: M = 3.20, SD = 3.29; $t(39) = -3.99$, $p = .001$) compared to recovered PCS patients.

6.5.3 Personality (Dispositional/Trait) Factors: Trait Anxiety, Neuroticism and Locus of Control

Independent samples t-tests showed significant differences in scores at the two months post-injury between patients categorized as having persistent PCS (PPCS) and patients recovered from PCS for trait anxiety and neuroticism (see table 10). There were no significant differences found between groups for locus of control.

6.5.4 Psychological (State) Factors: State Anxiety and Depression

Independent samples t-tests failed to show any significant differences between the PPCS and recovered PCS groups for state anxiety. However, significant differences in scores were found between the groups for depression (see table 10). Upon further scrutiny of the items in the BDI-II Inventory, the majority of the items appeared to derive from broad domains including cognition, affect and somatic concerns that are synonymous with aspects of neuroticism, a personality (dispositional/trait) factor. These aspects were guilt, anxiety and negative feelings towards self. To further explore this, an analysis was conducted using the factor structure of the BDI, namely- cognitive/affective and somatic factors according to Siegert, Walkey & Turner-Stokes (2009) whereby individual items were categorized according to the aforementioned factors and summed. The BDI-II for depression score was further analyzed according to its sub-factor structure, that is, cognitive/affect and somatic concerns. Independent t-tests showed significant differences between the PPCS group and recovered PCS group for both the cognitive/affect factor, $t(55) = -3.01$, $p = .004$, $d = -0.83$, and the somatic factor, $t(54) = -4.28$, $p = .001$, $d = -1.18$ in BDI-II.

Table 10: Means, SDs, t-test results and effect sizes for personality measures based on baseline assessment scores two months post-injury

Measures	Psychological and Personality Domains	Persistent PCS Patients (n = 34) *M* (*SD*)	Recovered PCS Patients (n = 23) *M* (*SD*)	*t*-value	*p* (2-tailed)	Effect size [a] (Cohen's *d*)
STAI	Trait Anxiety	48.53 (12.04)	40.39 (10.34)	-2.65	.01*	-0.73
NEO-FFI	Neuroticism	58.21 (10.20)	49.74 (11.12)	-2.97	.004**	-0.81
Rotter's Locus of Control Scale	Locus of Control	13.57 (3.94)	13.52 (3.38)	-0.04	.965	-
BDI-II	Depression	17.38 (12.11)	6.83 (8.79)	-3.811	.001**	-1.05
STAI	State Anxiety	39.94 (12.54)	33.87 (10.14)	-1.93	.06	-

[a]Effect sizes are calculated based on Thalheimer & Cook (2002).
* $p<.05$, ** $p<.01$.

6.6 Relationship of Trait and State Factors to PCS severity: Correlational Analyses

6.6.1 Injury/Neurogenic Factors: Neurocognitive Tests, GCS and Trauma

A moderate significant correlation was found between Rivermead PCS total score and trauma as measured by the Impact of Events Scale at $p < 0.01$. Low significant correlations were found for both Trail Making Test A and CVMT with Rivermead PCS total score at $p < 0.05$ for the baseline assessment. The remainder of the neurocognitive tests failed to correlate significantly with PCS total score. In addition, the correlation between GCS score and Rivermead PCS total score failed to reach significance. Table 11 shows the significant correlations between Rivermead PCS total score and injury/neurogenic factors.

Table 11: Correlations of injury/neurogenic factors with Rivermead PCS total score at baseline

	Impact of Events Scale	Trail Making Test A	CVMT
Rivermead PCS Total Score	.49**	.29*	-.30*

Note. N = 62.
* $p<.05$, ** $p<.01$.

6.6.2 Personality (Dispositional/Trait) and Psychological (State) Factors

Moderate to high significant correlations were found among Rivermead PCS total score, trait anxiety, neuroticism, state anxiety and depression at $p < 0.01$ for the baseline assessment two months post-injury (see table 12). The correlation between locus of control score and Rivermead PCS total score failed to reach significance. Correlation between state and trait anxiety at baseline assessment in patients recovered from PCS was high, $r(21) = .69$, $p < .01$.

However, the correlation of state and trait anxiety in patients with persistent PCS (PPCS) was higher at $r(32) = .80$, $p < .01$.

Table 12: Correlations of personality measures with Rivermead PCS total score at baseline

	Trait Anxiety	Neuroticism	State Anxiety	Depression
Rivermead PCS Total Score	.52**	.42**	.45**	.61**

Note. N = 62.
** $p<.01$.

6.7 Best Predictor of PCS: Regression Analyses

Regression analysis was performed on the MTBI patient sample at the baseline assessment with all variables that had a significant correlation with Rivermead PCS total score in order to identify the best predictor of PCS. Initial stepwise regression analysis elicited depression to be the only significant predictor of all the factors examined in the sample including injury (neurogenic), personality (dispositional/trait) and psychological (state) factors, $\beta = .59$, $t(53) = 5.22$, $p = .001$ and accounted for a significant proportion of the variance in the PCS total score, $R^2 = .35$, $F(1, 51) = 27.23$, $p = .001$. The BDI-II for depression score was further analyzed according to its sub-factor structure, that is, cognitive/affect and somatic concerns. Another stepwise regression analysis was performed with the inclusion of the scores from the 2 sub-factors with the other predictors. The total BDI-II score was excluded from this analysis. The results showed that the somatic factor in the BDI-II emerged as the best predictor of PCS, $\beta = .63$, $t(53) = 5.78$, $p = .001$ and accounted for a slightly higher significant proportion of the variance in the PCS total score, $R^2 = .40$, $F(1, 51) = 33.46$, $p = .001$, compared to the initial analysis.

CHAPTER 7: DISCUSSION

7.1 General Discussion

The objective of this study was to elucidate both injury (neurogenic) and non-injury (psychogenic) factors that influence post-concussive symptoms and its maintenance in people who have recently incurred a mild traumatic brain injury with a particular emphasis on the latter. Several injury, personality and psychological factors were scrutinized between healthy individuals and mild traumatic brain injury patients as well as across the post-concussive symptoms severity spectrum within MTBI patients over time. Finally, patients recovered from post-concussive symptoms were compared to patients still suffering from persistent PCS (PPCS) in an attempt to profile the former and latter groups.

In this unselected sample of mild traumatic brain injury survivors, nearly four fifths (79%) of patients had post-concussive symptoms at baseline assessment, and most (75.5%) had persistent symptoms at five months post-injury and eight months post-injury (79.5%). The findings from this study show that the 'moderate-severe' patients group consistently had higher scores compared to the 'no' and 'mild' symptoms groups in all the personality and psychological variables except in the locus of control measure for all three time points in the study. There has been no other study that compares PCS severity within MTBI patients to this extent in the literature thus far. There appears to be a clear positive linear relationship between personality and psychological variables with increasing severity of PCS. Overall, there were no significant changes in personality and psychological measures. Tests and instruments measuring injury factors did not predict PCS and persistent PCS except for the neurocognitive test, CVMT, in the visual memory domain and the findings that persistent post-concussive symptoms (PPCS)

patients were more likely to have been assaulted, have higher trauma levels about five months post-injury and abnormalities in CT scans compared to recovered PCS patients.

MTBI patients showed significantly greater severity of depression compared to healthy controls both clinically and statistically. Within the MTBI patients, there appeared to be a linear relationship suggesting that those who had a greater severity of post-concussive symptoms also had a higher propensity for anxiety and depression, as assessed by trait and state measures, compared to those with mild or no PCS. At five months post-injury, patients whose post-concussive symptoms persisted had greater trait anxiety, neuroticism and depression compared with those who had recovered from PCS. Litigation and compensation seeking status did not have an influence on PCS, neuroticism, depression and both state and trait anxiety at two months, five months and eight months post-injury in this sample.

7.2 Implications for the Etiology of PCS

7.2.1 Injury/Neurogenic Factors

The majority of injury factors did not relate significantly with post-concussive symptoms (PCS) and persistent post-concussive symptoms (PPCS). Amongst the neurocognitive tests, only the Continuous Visual Memory Test (CVMT) from the visual memory domain showed significant differences between comparison groups within MTBI patients, however, there were no significant differences in performance in the CVMT between MTBI patients and healthy controls. Tests assessing memory and attention have been consistently reported to show marked deficits in patients who have sustained a mild traumatic brain injury, however, such results have not been consistent in regard to PCS (Malhammar, 1967; Leininger, Gramling, Farrell, Kreutzer & Peck, 1990). Within the memory domain, verbal

and working memory ability compared to visual memory has shown greater impairment (Mathias, Beall & Bigler, 2004; Binder, 1986; Rimel et. al., 1981; Vanderploeg, Curtiss & Belanger, 2005). This finding may be related to information processing capacity, which is often reduced following MTBI and in patients experiencing PCS. Reduced information processing has been attributed to deficiency in one or more attentional subtypes such as simple, focused, selective, sustained and divided attention (Kay et. al, 1992; Kwok, Lee, Leung & Poon, 2008). Studies investigating word list recall tasks suggest difficulties in attention and encoding rather than actual retrieval of information (Raskin, Mateer & Tweeten, 1998; Sohlberg & Mateer, 2001). Therefore, the significant results found in the visual memory domain may be a manifestation of a primarily attention-related problem, which may be the reason why, although attention tests in this study did not show significant results, strong trends were observed. In addition, neurocognitive tests are generally accepted to be sensitive to cognitive impairments only in the early stages following an MTBI and are less effective as time from injury increases as most cognitive impairments resolve (Meares et al., 2006; Ponsford et al., 2000; Tay, Ang, Lau, Meyyappan & Collinson, in press). The MTBI sample in this study was assessed about fifty days (approximately two months) post-injury suggesting that most of the cognitive problems had already resolved.

One unexpected finding was seen in two significant interactions in Digit Span (working memory domain) and Category Verbal Fluency (executive functioning). Although the 'no' and 'moderate-severe' symptoms groups showed improvement in performance, the 'mild' symptoms group performed worse from the baseline assessment to the 3-month follow-up. This phenomenon may be attributable to the 'coping hypothesis'. According to the coping hypothesis, post-concussive symptoms (PCS) result from the chronic effort of patients to

compensate for their cognitive deficits that may elicit a chronic stress reaction (Bohnen, Jolles & Twijnstra, 1993; Bohnen, Jolles, Twijnstra, Mellink & Sulon, 1992). This stress reaction may undermine cognitive performance.

GCS, LOC and previous head injury were not significantly associated with PCS and PPCS in this sample. GCS and LOC are more predictive of outcome for severe forms of TBI, therefore this finding is consistent with most of the literature on MTBI (Dikmen et al., 1995). Research on mild TBI and PCS indicate previous head injury to be more likely in patients with persistent PCS (Ponsford et al., 2000), however this was not found in the present sample which could stem from smaller numbers of patients with a previous head injury (n = 18).

The results from this study also showed that people experiencing PPCS were more likely to be assaulted compared to people in the recovered PCS group. A study by Paterson et al. found a similar finding indicating that PPCS is most associated with people under the age of forty and who have been assaulted (2004). Trauma after MTBI was not significantly different between persistent PCS (PPCS) and recovered PCS groups at baseline assessment arguing against a psychological trauma explanation for PCS, however, there was a significant difference between groups at the 3-month follow-up with PPCS patients having higher avoidance and intrusion as well as total IES scores. The manifestation of trauma as late as about five months post-injury (at the time of the 3-month follow-up assessment) might represent the presence of PTSD as found by Bryant and Harvey who showed that MTBI patients with PTSD reported more PCS than MTBI patients without PTSD six months post-injury (1999). The manifestation of PTSD in the post-acute stage of MTBI may be related to injury factors such as PTA and LOC, which may act as a protective shield against re-experiencing trauma-related thoughts in the acute stage of MTBI (Bryant, 1996). However, PTA was not measured in this sample,

therefore it is not ascertainable. Another theory is that PTSD patients may have an attentional bias that causes selective attention to only negative symptoms (Bryant & Harvey, 1995). This may cause MTBI patients to be more aware of their symptoms leading to a further enhancement of their attentional bias. The aforementioned vicious cycle will maintain both PTSD and PCS in which case, the maintenance of PCS is not caused by the initial traumatic event.

There was a significant likelihood for PPCS patients to have MTBI-related anomalies on CT. Although the literature regarding the ability of CT scan to predict PCS and PPCS prediction is inconclusive (Iverson, Lange & Franzen, 2005, McCauley et al., 2001), it is generally accepted that structural brain damage visualized on CT and MRI scans increases the risk for slow or incomplete recovery (McCrea, 2008). The present findings support this view.

To summarize, the present study has elicited mostly non-significant results from the injury factors measured. GCS, LOC, previous head injury, and the majority of the neurocognitive tests did not show any relationship with PCS and PPCS. PPCS patients were more likely to have been assaulted, have abnormal CT scans and show evidence of psychological trauma as measured by the Impact of Events Scale (IES) relative to recovered PCS patients. This trauma did not manifest immediately after MTBI, but exhibited about five months post-injury. The manifestation of trauma after a relatively long period post-MTBI seems to suggest other perpetuating factors that may be linked to personality and/or psychological characteristics.

The present study did not measure the influence of metabolic factors such as biochemical markers (e.g. S-100B) and acute injury characteristics such as PTA in the manifestation of PCS. Results from the present study show that injury factors assessed are less determinative of PCS fifty days post-injury and PPCS approximately five months post-

injury. Therefore, the inclusion of metabolic factors and the measurement of PTA in this study are not considered to substantially change the outcome of the association of injury factors with PCS and PPCS as literature has shown that most injury factors are more indicative of short-term outcome (one to two weeks). As such, the utility of measuring injury/neurogenic indicators is limited in an MTBI sample with PCS problems persisting for more than one month. In view of the effect of MTBI-related trauma, the implications of these findings are suggestive that premorbid personality and psychological factors may offer an explanation of PCS after the immediate period of injury (approximately one month) and PPCS approximately three months post-injury.

7.2.2 Non-Injury (Personality and Psychological) Factors

7.2.2.1 Personality (Predispositional/Trait) Factors: Anxiety

In this study, a significantly high correlation between trait anxiety and PCS as well as unchanged levels of trait anxiety in MTBI patients at both five months and eight months post-injury strongly suggest that trait anxiety and PCS are related. Even though trait anxiety did not emerge as the best predictor of PCS, MTBI patients were consistently more anxious as PCS severity increased. In addition, the correlation between trait anxiety and state anxiety in PPCS patients was higher than that of recovered PCS patients suggesting high levels of baseline anxiety and thus implying that the PPCS patients were generally highly anxious overall. Furthermore, there was a strong trend for the ‘moderate-severe’ symptoms group to have higher trait anxiety score suggesting in part that the persistence of PCS may be related to a premorbid disposition.

At least one study has shown that premorbid anxiety, in terms of personality dispositions or psychiatric history exacerbates PCS (Moore et al., 2006). A sudden occurance such as an MTBI may disrupt the homeostasis between state and trait anxieties triggering commonly experienced symptoms such as free-floating anxiety, fearfulness, intense worry, generalised uneasiness, social withdrawal, interpersonal sensitivity and high-anxiety dreams (Alexander, 1995; Rao & Lyketsos, 2002). Anxiety levels in this sample were clinically as well as statistically significant with MTBI patients being more anxious than healthy controls by one standard deviation and PPCS patients being more anxious than recovered PCS patients by more than one standard deviation.

Premorbid anxiety along with PCS-like symptoms, have been reported in sample populations other than MTBI. Meares et al. found acute PCS in trauma patients who did not incur an MTBI at similar rates as those who did (2008). Furthermore, affective or anxiety disorders were associated with acute PCS (within 14 days post-injury) six times more than individuals without such complications regardless of the mode of trauma (Meares et al., 2008). PCS-like symptoms (e.g. headache, irritability and memory problems) were reported at high base rates in the normal, healthy population, especially amongst students following medical and psychological disorders (Iverson & McCracken, 1997; Sawchyn, Brulot & Strauss, 2000). Wang, Chan & Deng (2006) examined PCS in a group of 123 university students and investigated the relationship between symptom reporting and neuropsychological functioning and reported high base rates of PCS-like symptoms including fatigue, taking longer time to think, poor concentration, sleep disturbance and frustration in more than 45% of the total sample (Wang et al., 2006). However, unlike the present study, Wang et al. did not study the association of PCS in this population with anxiety. Lees-Haley, Fox & Courtney compared

complaints by MTBI and orthopedic injury patients and reported similar symptoms including being dazed, confused, dizzy, disoriented, having problems with concentration, numbness, and memory loss immediately after their injury (2001). Although PCS has been reported in sample populations such as orthopedic injury and other non-MTBI related trauma, the period between injury and PCS evaluation were in the acute post-injury phase (Landre, Poppe, Davis, Schmaus & Hobbs, 2006; Lees-Haley et al., 2001; Meares et al., 2008). It is unknown whether such PCS-like symptoms resulting from injuries unrelated to the brain persist for as long as the time points in the present study, which were fifty days (baseline assessment), about five months (3-month follow-up) and about eight months (6-month follow-up) post-injury. The closest study that assessed such symptoms in both MTBI and orthopedic injury patients longitudinally was in a sample of children and showed that MTBI is more likely than orthopedic injury to result in transient or persistent increases in PCS-like symptoms in the first year of injury (Yeates et al., 2009). Therefore, although PCS may be non-specific during the acute post-injury phase, it is unknown whether persisting symptoms beyond one month post-injury is characteristic of only MTBI and not other injuries unrelated to the brain.

A neuropsychological model has been developed to explain the brain mechanisms that may underlie the increased experience of anxiety after a MTBI by Gray and MacNaugton (1996). They suggest that activity in the "behavioural inhibition system" in the brain produces symptoms of anxiety. This system namely encompasses the septo-hippocampal system, anterior thalamus, 'Papez circuit', cingulate cortex, prefrontal cortex and the ascending noradrenergic fibres of the locus coeruleus (Gray & MacNaughton, 1996; Moore et al., 2006). Hence, individuals who are particularly vulnerable to anxiety and have an anxious disposition, have an excessively reactive behavioural inhibition system. The delocalised involvement of different

neural substrates and the complex, widespread neuronal pathways comprised in this system allows for a reasonable assumption that the behavioural inhibition system may be affected after MTBI and may contribute to persistent PCS (PPCS) (Moore et al., 2006).

Anxiety is especially relevant in Singapore with at least 10% of the population afflicted by some form of anxiety disorder (Health Promotion Board, 2004). The high prevalence of anxiety disorders in the population may be attributable to a socio-cultural and/or personality tendency to 'internalise' stress in some individuals coupled with environment influences such as Singapore's rigorous education system, national service, job demands, as well as high cost and standard of living (Lim et al., 2005; Lim, Mahendran & Low, 1997). Approximately 20% of the sample consisted of males who were in national service when the present study was conducted. National service in Singapore is the conscription of all male Singaporean citizens and second-generation permanent residents upon reaching the age of 18 (Ong, 2006). The serving period is two years as full-time national servicemen in the Singapore Armed Forces, Singapore Police Force, or the Singapore Civil Defence Force (MINDEF Singapore, 2009). Singapore is currently among a list of countries to have the longest military service exceeding 18 months, after Israel and South Korea, and used to have one of the longest mandatory military service periods, at thirty months prior to 2005 (Central Intelligence Agency, 2009). There is general dissent among young males regarding the length and utility of national service in Singapore (Nair, 2009). In addition, a study by Cheok et al. (2000) exploring rates of anxiety, depression and other psychological problems experienced by 77 male servicemen reporting to the Psychological Medicine Branch in the Singapore Armed Forces found the following prevalence rates of psychological problems: depression (28.6%), anxiety (22.1%), deliberate self-harm (13%), suicide ideation (7.8%), psychosis (9.1%) and poor work performance (5.2%). The

relatively high percentage of males serving national service in this sample (20%) and the internalized stress associated with conscription might explain the high rates of trait anxiety in male patients in general.

Studies have consistently shown that the female gender is associated with higher neuroticism and anxiety than males (Cattelani et al., 1996; Jardine, Martin & Henderson, 1984; Jorm, 1987). In this sample, however, the male gender elicited such findings. A plausible explanation for this result may be related to the dimension of culture called masculinity (Hofstede, 1980). According to Hofstede, gender differences are accentuated in masculine cultures like Japan and Austria where there is a stronger emphasis on occupational advancement and socio economic status (1998). Singapore is relatively similar to Japan in traditional gender values, therefore, stress caused by gender expectations as well as environmental circumstances applicable primarily only to males in Singapore, for example, national service, may explain the increased anxiety level.

Moreover, Singapore is more of a collectivistic rather than an individualistic society and research has found that collectivists, relative to individualists, have higher neuroticism, social anxiety, fear of failure, and use more avoidance-based coping strategies (Abe & Zane, 1990; Chang, 1996; Eaton & Dembo, 1997).

In this sample, about 39% of MTBI patients incurred their injury by falling or tripping closely followed by motor vehicle accidents (about 31%). The modalities by which MTBI was sustained in this sample may be related to personality, in particular, an accident-prone personality type (BBC Health, 2001; Juan, 2006; Marusic, Musek & Gudjonsson, 2001; Tillmann & Hobbs, 1949). Some research has shown that extraversion, sensitization, and an avoidance coping style are characteristics of accident-prone personality (Marusic et al., 2001).

In addition, people who score greater on psychoticism, neuroticism, and emotional coping are less likely to have thought about accident preventive measures (Marusic et al., 2001) and people low on both dependability and agreeableness, but high on openness are more likely to be susceptible to accidents as they have a lesser tendency to comply with instructions and are more easily distracted (BBC Health, 2001). These plausible personality features together with the high tendency of the Singapore population to possess a behavioural characteristic called 'kiasuism' may explain the injury modality distribution in this population (Ho, Ang, Loh & Ng, 1998). In essence, 'kiasuism' means the "fear of losing out to others" in Hokkien (a Chinese dialect). However, the motives underlying such behaviour are negatively connoted with anxiety, greed, envy and selfishness (Ho, Ang, Loh & Ng, 1998; Kirby & Ross, 2007).

The current population of examination is new and has educed interesting findings regarding the role of anxiety in the etiology of PCS and persistent PCS indicating that premorbid anxiety appears to increase the likelihood of PCS development.

7.2.2.2 Personality (Predispositional/Trait) Factors: Neuroticism

In this study, both MTBI and persistent PCS patients also had greater neroticism scores compared to healthy controls and recovered PCS patients respectively. In addition, male patients had greater neuroticism compared to healthy male controls. There have been no well-controlled studies to date that have explicitly investigated rates of neuroticism and its relationship to PCS in MTBI. The closest study approximated neuroticism level by gathering anecdotal accounts from relatives of the individuals who incurred MTBI (Keshavan et al., 1981). The difference in neuroticism levels in MTBI patients and comparison groups, that is,

healthy controls and sub-groups categorised by PCS severity is a novel finding. Neuroticism levels in the PPCS group and MTBI patients in general are higher than their respective comparison groups by at least one standard deviation making this finding clinically significant. Studies examining neuroticism and PCS in other populations are limited. Schneider investigated the role of neuroticism in post-injury mood disturbance in a sample of atheletes who incurred concussions and orthopedic injuries and found that the two variables were not significantly correlated (2006). The negative findings were attributed to limitations such as a low range of neuroticism scores within atheletes. Schneider, however, did not investigate PCS.

There is a considerable body of research to show that neuroticism is linked to anxiety (Costa & McCrae, 1985; Hettema, Prescott & Kendler, 2004; Jardine, Martin & Henderson, 1984; Matthews & Deary, 1998). Hettama, Prescott and Kendler found that there may be a substantial overlap in genetic factors which influence individual variation in neuroticism and those that increase the possibility of generalised anxiety disorder (2004). Hettama et al. conducted face-to-face or phone interviews in approximately 8000 male and female identical and fraternal twins to investigate general neuroticism levels and whether participants had an onset of generalized anxiety disorder at any point in their lives (Hettema, Prescott & Kendler, 2004). The researchers found that participants who scored high on neuroticism also experienced generalized anxiety disorder. Furthermore, the coexistence of neuroticism and generalized anxiety disorder occurred more often in identical twins that share 100 percent of genes than in fraternal twins that share 50 percent of genes (Hettema, Prescott & Kendler, 2004). Given that neuroticism is considered to be a stable trait in personality, the findings from the present study point to a predispositional cause for the rate and persistence of PCS (Fox, Lees-Haley, Earnest, Dolezel-Wood, 1995).

7.2.2.3 Related Personality (Predispositional/Trait) Factors: Locus of Control

Locus of control was significantly higher in patients compared to controls but did not differ within the MTBI sample according to PCS severity, and between PPCS and recovered PCS groups. There have been trends observed in a few studies where an individual's perception of his/her influence over an accident affects the emergence, severity and duration of PCS (Lishman, 1988). Significantly more PCS were reported by people who could attach blame to an external body such as an employer or a large organisation as compared to people who blamed themselves. In other words, people with high external locus of control had greater likelihood of PCS as opposed to people with high internal locus of control (Lishman, 1988; Rutherford, Merrett & McDonald, 1977). The difference in locus of control scores between MTBI patients and healthy controls is a novel finding implying that people who incur an MTBI and have persistent post-concussive symptoms (PPCS) attribute happenings in their lives to externalities.

7.2.2.4 Psychological (State) Factors: Depression

The most consistent finding of the present study was that state depression was significantly greater clinically and statistically in MTBI patients, the 'moderate-severe' group of patients and persistent PCS patients in this study. Furthermore, it was found that depression severity improved in 'mild' and 'moderate-severe' symptoms groups at five months post-injury, but increased at eight months post-injury.

Research examining depression in relation to PCS is inconclusive. Some studies show that depression has a significant role in the manifestation of PCS while others find no

relationship (Busch & Alpern, 1998; Cicerone & Kalmar, 1997; Schoenhuber & Gentilini, 1988). In addition, both positive and negative studies are limited by methodological concerns including differing criteria in defining MTBI and depression, differences in time elapsed since brain injury and control group variations that confound comparisons (Busch & Alpern,1998). The present study is methodologically better in terms of using well cited definitions and measures for the assessment of MTBI and depression, having adequate participant numbers in comparison groups and ensuring no significant variations in age and education in the comparison groups.

It is established that serotonin level affects depression (Caspi et al., 2003; Kalat, 2008; van Praag, 1981). Neuroendocrine studies have shown that patients with diffuse cerebral injuries had similar levels of homovanillic acid, a marker of serotonin, compared to controls and frontotemporal injury patients, but their levels of 5-HIAA (suggesting serotonergic involvement) were higher than both the controls and frontotemporal patients (Van Woerkom, Teelken & Minderhoud, 1977). In addition, studies have shown a significant association between major depressive episodes and lesion location (left dorsolateral frontal and/or left basal ganglia, and to a lesser degree parietal-occipital and right hemispheric lesions) (Busch & Alpern, 1998). Interestingly, anxiety problems are also more common in left hemisphere damage compared to right hemisphere damage (Epstein & Ursano, 1994).

The findings from the present study show that depression plays a clear role in the manifestation of PCS, which is consistent with some research in this area (King, 1996; McCauley et al., 2001; Schoenhuber & Gentilini, 1988). However, the directionality of the association between depression and PCS, that is, whether PCS is driving symptoms of

emotional distress or vice versa was not explored in this study and has been discussed as part of future directions.

The observation where depression in the 'mild' symptoms group improved at the second time point and worsened at the third may be attributed to a bimodal phenomenon whereby depression symptoms increased in severity when PCS was perceived to worsen. This type of depression is similar to 'reactive depression' where the depressive symptoms are precipitated by a current situation (Beck & Alford, 2009). Thus, the rumination about post-concussive symptoms could cause a chronic stress reaction, much like the reaction in the 'coping hypothesis' whereby PCS is viewed as compensation for deficits in functioning caused by brain injury (Bohnen, Jolles & Twijnstra, 1992; Bohnen, Jolles, Twijnstra, Mellink & Sulon, 1992). Furthermore, changes in neuroendocrine levels caused by the direct effects of brain injury are likely to exacerbate depression in MTBI, PCS and persistent PCS patients. It is also noteworthy that cognitive performance in the Digit Span test and Category Verbal Fluency test was worse at time point two compared to time point one in the 'mild' symptoms group. Therefore, it appears that the 'mild' symptoms group was not adjusting well post-injury, their functional shortcomings exacerbating both PCS and depression through a vicious cycle.

7.2.2.5 Related Psychological (State) Factors: State Anxiety

Significant differences in state anxiety did not emerge between recovered PCS and PPCS groups, however, MTBI patients had significantly higher state anxiety compared to healthy controls and state anxiety was significantly greater in the 'moderate-severe' PCS group. Upon closer scrutiny of state anxiety scores, it was found that state anxiety levels in this sample

were comparable to the existing norms. The greater trait anxiety and normal state anxiety levels in MTBI patients suggests that the type of anxiety that affects the expression of PCS is primarily dispositional/trait-based and premorbid in nature.

7.2.3 PCS as a Psychosomatic Disorder

This study systematically explored depression according to a two-factor structure, that is, cognitive/affect and somatic concerns. The somatic concerns factor was the best predictor of PCS in this sample and the effect size for somatic concerns was higher than that of cognitive/affect in persistent PCS patients. Many studies have considered the manifestation of somatic complaints in PCS as part of a coping mechanism in patients who continue to experience difficulties in resuming normal daily activities (Nicholson, 2000). Others acknowledge that there is a significant association between somatic conditions of chronic pain, sleep disturbance and persistent PCS (Alexander, 1995; Larrabee, 1997; Nicholson, 2000). Somatisation is considered to be a form of physical manifestation of inherent psychological distress relating to anxiety and depression (Lipowski, 1988; Olatunji, Deacon, Abramowitz & Tolin, 2006). A longitudinal study examining symptoms of somatization and depression in an initially healthy cohort of community adults revealed that baseline somatization score significantly predicted self-reported symptoms of depressed mood five years after the initial assessment, but only in women (Terre, Poston, Foreyt & St Jeor, 2003). Furthermore, another study by Jakupcak et al. comprising of 45 male veterans seeking inpatient treatment for posttraumatic stress disorder (PTSD) found that PTSD severity, depression symptom severity and anxiety sensitivity were each positively and significantly related to veterans' self-reported severity of somatic complaints (2006). In the aforementioned study, the results of a hierarchical regression analysis indicated that anxiety and depression severity account for the relationship

between PTSD and somatic complaints, suggesting that PTSD influences somatic complaints by virtue of underlying symptoms of depression and anxiety sensitivity (Jakupcak et al., 2006). In view of these findings, it is useful to consider somatization as an entity that connects depression and anxiety, both of which are very relevant to the genesis of PCS and persistent PCS as shown by literature and the results in this study (Mooney & Speed, 2001). Furthermore, depression and anxiety are not mutually exclusive in that they commonly emerge as comorbid disorders in psychiatric diagnoses. The strong relationship between anxiety and depression in this study is further corroborated by high significant correlations found between them and amongst the other personality and psychological variables with PCS. Thus, the present study strongly suggests that anxiety, at least within an Asian population, is at the crux of the etiology of post-concussive symptoms and is closely related to personality and psychological variables such as somatization, neuroticism and depression which account for the persistence of post-concussive symptoms.

7.3 Limitations

This study did not involve a consecutive series of patients with MTBI. Instead, the sample consisted of patients who returned for their follow-up appointment at the Mild Head Injury Clinic. For this reason, there is a potential selection bias in the process by which subjects were enrolled into the study. However, this sample is more likely to reflect those individuals who do not recover and have ongoing impairments for which they seek assistance making it a suitable sample for the examination of persistent PCS.

The sample size for the subgroup analyses based on severity of symptoms was relatively small. However, studies in this area of research, that is mild head injury and in particular PCS

have similar sample sizes or even smaller sample sizes (Rapoport, Kiss & Feinstein, 2006, King, Crawford, Wendon, Caldwell & Wade, 1999). The pattern of findings in these similar studies also emulate the present study's findings to a certain extent, especially for the neurocognitive tests in that non-significant effects were found. However given these small sample sizes, significant main effects were persistently elicited majority of the time in the personality and psychological tests, which adds further strength and support to the findings.

This study mostly consisted of patients who incurred their MTBI injuries from falls or tripping. Most other studies in the literature consist of patients who sustained an MTBI from a motor vehicle accident. The injury profile of this sample may be characteristic of the population in Singapore. Longer study duration may change the injury profile of the sample to be consistent with the majority of studies.

The present study was also not prospective in that it used retrospective measures of personality. It would have been better if baseline personality traits were assessed before MTBI; however, such large-scale assessment is virtually impossible unless it is done in the manner of normative studies.

This study did not collect data and information on biochemical markers or metabolic factors, PTA, lesion location and MRI scans to correlate with physical damage. The collection of the aforementioned indicators would have lead to a more definite conclusion on the role of injury factors in the manifestation of PCS. However, even without such indicators, the present study was able to show the greater contribution of anxiety and other personality/psychological factors in the manifestation and persistence of PCS compared to injury factors. Furthermore, MRI studies in MTBI research have sometimes been noted to elicit no value-adding contribution to the extant literature (Hammoud & Wasserman, 2002; Iverson, Lange, Gaetz &

Zasler, 2006).

The final limitation of the present study is that there was no control group that consisted of patients who had other forms of trauma such as orthopedic injury or chronic pain. Such inclusion of another comparison group would have assisted in the better delineation of whether PCS and persistent PCS are primarily a mild traumatic brain injury phenomenon or a non-specific clinical entity.

7.4 Future Directions

Further research should explore the role of trait depression in PCS and explore whether the emergence and maintenance of PCS and persistent PCS is a manifestation of premorbid personality factors more so than psychological factors, that is, more trait-based than state-based. This distinction can tailor appropriate intervention strategies that arrest the complete manifestation of PCS or reassure patients about normal and abnormal recovery periods after MTBI.

Presently few studies have investigated the potential for anxiety and depression alleviating psychological interventions in the treatment of PCS. Most anecdotal evidence suggests that education about the benign effects of MTBI, reassurance that symptoms are not indications of permanent brain damage and managed resumption of premorbid activities are important in effecting good outcome. At least one study has shown that PCS rates are higher when patients are given no information about their symptoms (Kelly, 1975) but few studies have systematically addressed the role of psycho-education in treating PCS, or in elucidating the role of psycho-education as a means of reducing or even preventing anxiety and depression post-MTBI. Studies that have investigated such approaches lack appropriate methodological controls such as prospective design, blind/random group assignment and systematised outcome measures (Mittenberg, Tremont, Fichera, Zielinski & Rayls, 1996; Comper, Bisschop, Carnide & Tricco, 2005). One relevant exception is Mindehoud et al. (1980) who reported retrospective outcome data on patients who were given a printed manual that consisted of information about the nature, cause and expected recovery of symptoms and a program of gradual resumption of work or school/university activities. Those treated demonstrated significantly fewer PCS symptoms 6 months post-MTBI than those who did not receive information. However, the

authors could not clarify the underlying reasons for the success of their program or detail the component(s) and component interactions between premorbid disposition, reaction types and the role of information in offsetting long term psychological morbidity. The present study has collected psychoeducation based intervention data in a more methodologically well-controlled study design compared to previous studies. Data analysis is currently ongoing to further understand coping strategies which are suitable for the rehabilitation of mild traumatic brain injury patients suffering from post-concussive symptoms (PCS) and persistent post-concussive symptoms (PPCS).

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Appendices

1. Self-Constructed Demographic Questionnaire
2. Conferences attended and published abstracts

1. Self-Constructed Demographic Questionnaire

Demographic Information
Instructions: Please answer the following questions and circle the appropriate responses.

1. Have you ever had an injury, which resulted in unconsciousness before this accident? **Yes/No**
   If Yes, details of injury (How many previous injury, When, type of accident, when treated, how long was treatment, whether still on treatment?)

_____
_____
_____

2. Have you ever had any of the following? (Please tick in the box(es).)
   - □ Depression/Low mood
   - □ Anxiety
   - □ Hear voices in your head that talk to you or order you to do things?
   - □ See things that other people do not see?
   - □ Complaints of pain in parts of your body that cannot be accounted for by physical injury?

3. Have you had a history of mental illness or seen a doctor/psychiatrist for any mental health problem? **Yes/No**
   If Yes, what was it? _____
   If Yes, at what age did it happen? _____
   If Yes, how long did it last for? _____
   If Yes, did you undergo any treatment for it? _____
   If Yes, are you still suffering from it? **Yes/No**

4. Do you drink alcohol? **Yes/No**
   If Yes, what do you drink? _____
   How many glasses/cans of alcohol do you drink per week? _____

5. Highest level of education: Primary/ Secondary/ Tertiary/ Post-Tertiary
   No of years of education: _____ years

6. Current Occupation : _____

7. Contact Details: _____

2. Conferences attended and published abstracts

I. 7th World Congress on Brain Injury organized by the International Brain Injury Association in Lisbon, Portugal (2008):

Collinson, S., **Meyyappan, A.**, & Ang, C. B. T. (Published Online: 2008). The role of anxiety in the emergence, severity and maintenance of post-concussive syndrome (Abstract). Brain Injury, Volume 22, Suppl 1. DOI:10.1080/02699050801984334, http://www.informaworld.com.libproxy1.nus.edu.sg/smpp/section?content=a791715345&fulltext=713240928

II. INS Mid-Year Meeting 2009 organized by the International Neuropsychological Society and the Finnish Neuropsychological Society in Helsinki, Finland and Tallinn, Estonia (2009):

Meyyappan, A., Tay, S., Lau, E., Ang, B. T., & Collinson, S. L. (Published Online: 2009). Relationship of trait anxiety and personality factors with post-concussive syndrome (PCS) following mild traumatic brain injury (MTBI). (Abstract). Journal of the International Neuropsychological Society, Volume 15, Suppl 2. DOI:10.1017/S1355617709991044, http://journals.cambridge.org/action/displayFulltext?type=1&pdftype=1&fid=6385556&jid=INS&volumeId=15&issueId=S2&aid=6385552